

CHARACTERISTICS OF REPRODUCTIVE DISORDERS IN WOMEN WITH TYPE 1 DIABETES MELLITUS LIVING IN CONDITIONS OF SEVERE IODINE DEFICIENCY IN THE FERGANA REGION

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Abstract

Type 1 diabetes mellitus (T1DM) is one of the most significant endocrine disorders affecting women of reproductive age and is associated with numerous metabolic, hormonal, and reproductive complications. In regions characterized by severe iodine deficiency, additional endocrine disturbances may further aggravate reproductive dysfunction. The Fergana region has historically been recognized as an area with insufficient iodine intake, leading to widespread thyroid abnormalities among the population. The coexistence of T1DM and iodine deficiency may create a complex endocrine environment that negatively influences ovarian function, menstrual regularity, fertility, and pregnancy outcomes. This study aimed to investigate the characteristics of reproductive disorders in women with T1DM living under conditions of severe iodine deficiency in the Fergana region. A comprehensive clinical, hormonal, and ultrasonographic assessment was conducted among reproductive-aged women diagnosed with T1DM. The study evaluated menstrual disturbances, ovarian dysfunction, infertility prevalence, thyroid status, metabolic control, and reproductive hormone profiles. The findings demonstrated a high frequency of menstrual irregularities, delayed puberty, anovulation, infertility, thyroid dysfunction, and adverse reproductive outcomes among women with T1DM residing in iodine-deficient areas. Poor glycemic control and thyroid hormone imbalance were strongly associated with reproductive abnormalities. The study highlights the necessity of integrated endocrine monitoring, optimization of metabolic control, and iodine deficiency correction to improve reproductive health in this vulnerable population.

Keywords: Type 1 diabetes mellitus, iodine deficiency, reproductive disorders, infertility, menstrual dysfunction, thyroid hormones, ovarian function, endocrine disorders, fertility, Fergana region.

1. Introduction

Type 1 diabetes mellitus is a chronic autoimmune disease characterized by destruction of pancreatic β -cells and absolute insulin deficiency. Although substantial advances have been achieved in diabetes management over recent decades, reproductive complications remain a significant concern among

women with T1DM. The female reproductive system is highly sensitive to metabolic disturbances, and chronic hyperglycemia can adversely affect hypothalamic-pituitary-ovarian axis regulation, ovarian reserve, ovulation, and fertility.

Women with T1DM frequently experience reproductive abnormalities, including delayed menarche, menstrual irregularities, polycystic ovarian changes, luteal phase defects, infertility, and adverse pregnancy outcomes. These complications result from multiple mechanisms involving insulin deficiency, hyperglycemia, oxidative stress, endothelial dysfunction, and alterations in reproductive hormone secretion. Furthermore, autoimmune thyroid diseases are considerably more common among women with T1DM than in the general population, creating additional endocrine challenges. Iodine is an essential micronutrient required for thyroid hormone synthesis. Severe iodine deficiency remains an important public health issue in several regions of Central Asia, including parts of Uzbekistan. The Fergana region has long been recognized as an endemic area for iodine deficiency disorders due to environmental and nutritional factors. Inadequate iodine intake leads to decreased thyroid hormone production, thyroid enlargement, hypothyroidism, and disturbances in reproductive physiology.

Thyroid hormones play a crucial role in maintaining normal reproductive function. They influence gonadotropin secretion, ovarian follicular development, steroidogenesis, endometrial receptivity, and pregnancy maintenance. Consequently, women exposed to chronic iodine deficiency frequently experience menstrual disorders, infertility, miscarriage, and obstetric complications. When iodine deficiency coexists with T1DM, reproductive dysfunction may become more severe because both conditions independently affect endocrine regulation.

The interaction between diabetes-related metabolic abnormalities and thyroid dysfunction caused by iodine deficiency has not been sufficiently investigated in women living in endemic regions. Understanding the reproductive consequences of this combined endocrine burden is essential for developing targeted preventive and therapeutic strategies.

The aim of this study was to investigate the clinical and hormonal characteristics of reproductive disorders in women with type 1 diabetes mellitus living under conditions of severe iodine deficiency in the Fergana region.

2. Materials and Methods

A cross-sectional observational study was conducted involving 120 women of reproductive age diagnosed with type 1 diabetes mellitus and residing in iodine-deficient districts of the Fergana region. The study was performed in specialized endocrinology and gynecology departments between 2022 and 2025.

The inclusion criteria consisted of confirmed T1DM diagnosis for at least three years, age between 18 and 40 years, permanent residence in the Fergana region, and informed consent for participation. Exclusion criteria included pregnancy at the time of examination, severe chronic systemic diseases unrelated to diabetes, malignant disorders, and previous reproductive surgeries affecting fertility. The participants were divided into two groups according to glycemic control. Group 1 included 62 women with satisfactory metabolic control (HbA1c below 7.5%), while Group 2 consisted of 58 women with poor glycemic control (HbA1c above 7.5%).

Clinical evaluation included collection of demographic data, diabetes duration, insulin therapy characteristics, body mass index, reproductive history, age at menarche, menstrual cycle patterns, fertility status, pregnancy outcomes, and history of thyroid disease.

Laboratory investigations included fasting plasma glucose, glycated hemoglobin, thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), anti-thyroid peroxidase antibodies, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, progesterone, prolactin, testosterone, and anti-Müllerian hormone (AMH). Urinary iodine concentration was measured to assess iodine status.

Ultrasonographic examination of the thyroid gland was performed to determine thyroid volume, structural abnormalities, and the presence of nodular formations. Pelvic ultrasound evaluation included assessment of ovarian morphology, follicular development, endometrial thickness, and uterine characteristics.

Statistical analysis was conducted using standard biomedical statistical methods. Quantitative variables were expressed as mean $\pm$ standard deviation. Comparative analyses between groups were performed using Student's t-test and chi-square test.

3. Results

The mean age of the participants was 28.4 ± 5.7 years. The average duration of diabetes was 11.2 ± 4.8 years. Urinary iodine measurements confirmed severe iodine deficiency among the majority of study participants, with mean urinary iodine concentration significantly below recommended levels.

Delayed menarche was identified in 38.3% of women. The average age at menarche among participants was significantly higher than reported regional averages for healthy women. Menstrual irregularities were documented in 61.7% of patients and included oligomenorrhea, secondary amenorrhea, polymenorrhea, and irregular menstrual cycles.

Among women with poor glycemic control, menstrual disturbances occurred significantly more frequently than among those with satisfactory metabolic control. Oligomenorrhea was observed in 34.5% of patients, while secondary amenorrhea affected 15.8%.

Hormonal analysis demonstrated elevated TSH levels and reduced FT4 concentrations in a substantial proportion of women. Subclinical hypothyroidism was identified in 29.2% of participants, while overt hypothyroidism was diagnosed in 13.3%. Autoimmune thyroiditis markers were positive in 26.7% of examined women.

Abnormal ovarian function was observed in 52.5% of participants. Anovulatory cycles were detected in 41.7% of women, while luteal phase insufficiency occurred in 35.8%. Reduced progesterone levels during the luteal phase indicated impaired ovulatory function and compromised fertility potential. Ultrasound examination revealed polycystic ovarian morphology in 22.5% of cases. Reduced ovarian volume and diminished follicular reserve were observed more frequently among women with longer diabetes duration and poor metabolic control.

Infertility was diagnosed in 27.5% of married participants. Primary infertility accounted for 57.6% of infertility cases, while secondary infertility represented 42.4%. Women with combined diabetes and thyroid dysfunction demonstrated significantly higher infertility rates compared with those having normal thyroid function.

Pregnancy history analysis revealed elevated frequencies of spontaneous abortion, fetal growth restriction, preterm birth, and gestational complications. Women with poor glycemic control and severe thyroid dysfunction experienced the highest rates of adverse reproductive outcomes. Correlation analysis demonstrated significant associations between HbA1c levels and menstrual abnormalities, infertility risk, and hormonal disturbances. Elevated TSH concentrations were independently associated with ovulatory dysfunction and reduced fertility indicators.

4. Discussion

The present study demonstrated that reproductive disorders are highly prevalent among women with T1DM living in conditions of severe iodine deficiency. The combination of chronic metabolic dysregulation and thyroid hormone insufficiency appears to exert a profound negative impact on reproductive physiology.

The observed delay in menarche among women with T1DM is consistent with the known effects of insulin deficiency and chronic hyperglycemia on pubertal development. Insulin plays a fundamental role in growth and maturation processes, and inadequate metabolic control may delay activation of reproductive endocrine pathways.

Menstrual disturbances represented one of the most common reproductive abnormalities identified in the study population. Chronic hyperglycemia can impair hypothalamic gonadotropin-releasing hormone secretion, resulting in abnormal pituitary gonadotropin release and disrupted ovarian function. Simultaneously, hypothyroidism caused by iodine deficiency may further alter gonadotropin secretion and ovarian steroidogenesis.

The high prevalence of thyroid dysfunction observed in this study confirms the significant endocrine burden experienced by women residing in iodine-deficient areas. Thyroid hormones regulate multiple aspects of reproductive function, including follicular growth, ovulation, implantation, and maintenance of pregnancy. Therefore, thyroid dysfunction substantially contributes to infertility and adverse obstetric outcomes.

The increased frequency of anovulation and luteal phase defects suggests impaired ovarian endocrine activity. These findings may be explained by metabolic stress, oxidative damage, vascular abnormalities, and hormonal imbalances associated with both T1DM and iodine deficiency.

Infertility rates among study participants exceeded those reported for the general female population.

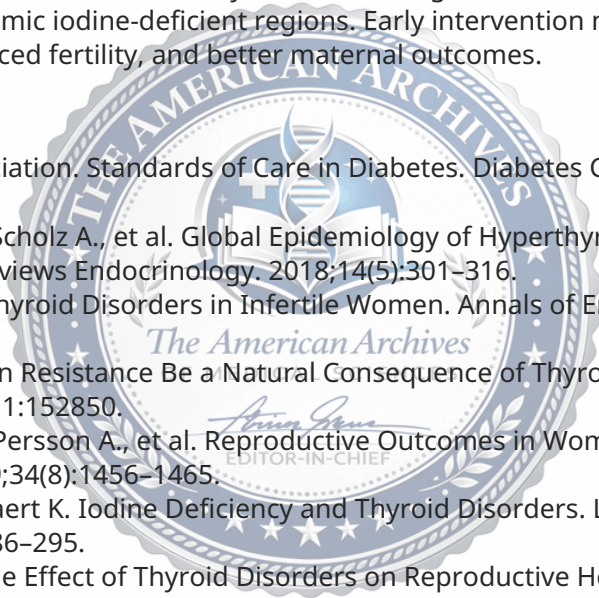
This observation highlights the cumulative negative effects of diabetes-related complications and thyroid dysfunction on reproductive capacity. Women with poor glycemic control exhibited the most severe reproductive disturbances, emphasizing the importance of optimal diabetes management. The relationship between elevated HbA1c levels and reproductive dysfunction supports previous evidence indicating that chronic hyperglycemia directly affects ovarian reserve, follicular maturation, and endometrial receptivity. Likewise, elevated TSH concentrations were associated with reduced fertility indicators, further confirming the reproductive significance of thyroid hormone homeostasis. These findings underscore the necessity of multidisciplinary care involving endocrinologists, gynecologists, reproductive specialists, and public health professionals. Early diagnosis and treatment of thyroid dysfunction, together with improved glycemic control and iodine supplementation programs, may significantly enhance reproductive outcomes among affected women.

5. Conclusion

Women with type 1 diabetes mellitus living under conditions of severe iodine deficiency in the Fergana region exhibit a high prevalence of reproductive disorders, including delayed menarche, menstrual irregularities, anovulation, infertility, and adverse pregnancy outcomes. Thyroid dysfunction resulting from chronic iodine deficiency further exacerbates reproductive impairment and negatively influences fertility potential. Poor glycemic control significantly increases the risk and severity of reproductive abnormalities. Comprehensive reproductive assessment, strict metabolic control, regular thyroid monitoring, and correction of iodine deficiency should be integrated into the management of women with T1DM residing in endemic iodine-deficient regions. Early intervention may contribute to improved reproductive health, enhanced fertility, and better maternal outcomes.

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