American Journal of Medicine and Medical Sciences 2026, 16(3): 1276-1279
DOI: 10.5923/j.ajmms.20261603.88

Clinical Characteristics of Postoperative Complications in Patients with Diffuse Toxic Goiter and Recurrent Disease

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Abstract The aim of the study was to investigate the characteristics of postoperative complications in patients with diffuse toxic goiter and disease recurrence. Clinical data were collected at the City Clinical Hospital No. 1 in Andijan. A total of 62 patients were examined, including 42 women and 20 men. The mean age was 49.2 ± 1.62 years (47 ± 1.76 years in women and 42 ± 2.6 years in men). Among the 62 patients with diffuse toxic goiter (DTG) who received conservative treatment, 47 patients achieved complete remission. Of these 62 patients, 19 (30.6%) had mild thyrotoxicosis, 28 (45.2%) had moderate thyrotoxicosis, and 15 (24.2%) had severe thyrotoxicosis. In 15 patients (24.2%), disease recurrence was observed two years after conservative treatment. Due to recurrence, these patients underwent total strumectomy. Thus, 47 patients formed the main group (drug therapy), while 15 patients constituted the recurrence group (drug therapy plus strumectomy). The control group consisted of 20 healthy individuals (10 women and 10 men), whose hormonal parameters were used to assess the reliability of the obtained results. **Research methods** included general clinical, biochemical tests (bilirubin – total, direct and indirect, ALT, AST, prothrombin index, coagulogram, C-reactive protein), hormonal tests (TSH, free thyroxine, antibodies to TSH receptors, and prolactin in blood), anthropometric measurements (height (cm), weight (kg), body mass index (BMI, kg/m^3), waist circumference, hip circumference), and instrumental methods such as ECG, echocardiography, ultrasound examination of the thyroid gland and internal organs, and chest X-ray. The study demonstrated that the most pronounced immunohormonal disturbances were observed in patients with severe thyrotoxicosis. This group included patients with disease recurrence during conservative treatment who subsequently underwent surgical treatment. In patients of the recurrence group, one month after total strumectomy in the postoperative period, as well as in patients of the conservative treatment group, compensation of the condition and the development of postoperative hypothyroidism were observed. After traditional treatment in the main group, remission was achieved in 47 (75.4%) patients, whereas after the use of a comprehensive conservative method remission was achieved in 15 (26.2%) patients. Changes in the titers of antibodies to TSH receptors during treatment may be useful for predicting relapse after treatment with antithyroid drugs in patients who had positive antibodies to TSH receptors at the time of diagnosis.

Keywords Diffuse toxic goiter, Strumectomy, Postoperative complications

1. Introduction

Treatment options for Graves' disease or diffuse toxic goiter (DTG) after a course of antithyroid therapy remain a challenging task for individualized patient management. Currently, there is no single index to determine which patients respond better to antithyroid therapy and achieve remission after treatment. Due to their active pathogenic role, the measurement of antibodies to the thyroid-stimulating hormone receptor (TRAb) at the time of discontinuation of antithyroid therapy is used as a predictor of relapse in Graves' disease; however, published data remain contradictory [1].

Received: Feb. 22, 2026; Accepted: Mar. 16, 2026; Published: Mar. 23, 2026
Published online at http://journal.sapub.org/ajmms

Graves' disease (GD) is an autoimmune disorder of the thyroid gland caused by antibodies that stimulate the thyroid-stimulating hormone (TSH) receptor on thyroid follicular cells [1]. One of the standard treatment approaches for GD is the administration of antithyroid drugs (ATDs) for 12–18 months [2]. This treatment may lead to remission of the disease without the development of subsequent hypothyroidism. However, the risk of relapse remains high, and patients may experience adverse effects [2].

Antithyroid drugs may also exert immunomodulatory effects associated with normalization of TSH receptor antibody (TRAb) levels over time, which may be important for achieving remission after therapy [3]. In addition, changes in thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies (TgAb) during ATD treatment have also been reported [4]. The remission rate varies depending

on ethnicity and geographical region [5]. In patients with normalized TRAb levels, the relapse rate ranges from 20% to 30% during 3–5 years of follow-up [1]. Overall, the risk of relapse after a 1–2-year course of ATD therapy is approximately 50% [6,7].

Previously identified predictors of relapse include young age, larger goiter size, smoking, male sex, severe hyperthyroidism, higher antibody concentrations, and the presence of Graves' ophthalmopathy [2,7,8,9]. The usefulness of measuring TRAb at the time of ATD withdrawal for predicting subsequent relapse of hyperthyroidism has been extensively studied [10–13]. However, the influence of TPOAb on the course of Graves' disease after discontinuation of ATD therapy remains unclear.

The aim of this study was to investigate the effect of autoimmune antibodies on the risk of recurrence of Graves' disease in patients treated with antithyroid drugs.

Aim of the study: to investigate the characteristics of postoperative complications in patients with diffuse toxic goiter and disease recurrence.

2. Materials and Methods

Clinical data were collected at the City Clinical Hospital No. 1 in Andijan. A total of 62 individuals were examined, including 42 women and 20 men. The mean age of the participants was 49.2 ±1.62 years (47 ±1.76 years in women and 42 ±2.6 years in men).

Among the 62 patients with diffuse toxic goiter (DTG) who received conservative treatment, 47 patients achieved complete remission. Of the total number of patients, 19 (30.6%) had mild thyrotoxicosis, 28 (45.2%) had moderate thyrotoxicosis, and 15 (24.2%) had severe thyrotoxicosis. In the remaining 15 patients (24.2%), disease recurrence was observed two years after conservative treatment, and therefore these patients underwent total strumectomy.

Thus, 47 patients constituted the main group (drug therapy), while 15 patients formed the recurrence group (drug therapy combined with strumectomy).

The control group consisted of 20 healthy individuals (10 women and 10 men), whose hormonal parameters were used to assess the reliability of the obtained results.

Inclusion criteria

Diffuse toxic goiter; male and female patients.

Exclusion criteria

Patients with carbohydrate metabolism disorders, ischemic heart disease, heart defects, idiopathic cardiomyopathies, as well as patients with a history of cerebrovascular accidents were not included in the study.

Research methods

The study included general clinical, biochemical, hormonal, anthropometric, and instrumental methods.

Biochemical tests included total, direct, and indirect bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), prothrombin index (PTI), coagulogram, and C-reactive protein (CRP).

Hormonal tests included thyroid-stimulating hormone (TSH), free thyroxine (fT4), antibodies to TSH receptors (TRAb), and prolactin levels in blood.

Anthropometric measurements included height (cm), weight (kg), body mass index (BMI, kg/m^2), waist circumference, and hip circumference.

Instrumental examinations included electrocardiography (ECG), echocardiography (Echo-ECG), ultrasound examination of the thyroid gland and internal organs, and chest X-ray.

The baseline examination of patients included medical history collection (patient complaints, time of their first appearance, possible causes according to the patient, time of first medical consultation, time of diagnosis, type of therapy received and its effectiveness), physical examination (heart rate and blood pressure measurement), and general clinical examinations.

Hormonal status was assessed by determining free triiodothyronine (fT3), free thyroxine (fT4), and thyroid-stimulating hormone (TSH). To clarify the autoimmune nature of the disease, the titer of antibodies to TSH receptors (TRAb) was determined. Hormonal levels were measured in blood serum using reagents produced by HUMAN (Germany).

The obtained data were statistically processed on a personal computer (Pentium-IV) using the Microsoft Office Excel-2003 software package, including built-in statistical functions. Methods of parametric and non-parametric variation statistics were applied with calculation of the arithmetic mean (M), standard deviation (SD), standard error of the mean (m), and relative values (frequency, %). Statistical significance of differences between mean values was determined using Student's t-test with calculation of the probability of error (P), after testing the normality of distribution (kurtosis test) and equality of variances (Fisher's F-test). Differences were considered statistically significant at $\mathbf{P < 0.05}$.

3. Results

The distribution of patients by age groups is presented in **Table 1**.

From **Table 1**, it can be seen that the majority of patients were observed in the age group of **31 to 50 years**, both among men (35.7%) and women (64.3%).

Among the 62 patients with diffuse toxic goiter (DTG) who received conservative treatment, 47 patients achieved complete remission. Of the total number of patients, 19 (30.6%) had mild thyrotoxicosis, 28 (45.2%) had moderate thyrotoxicosis, and 15 (24.2%) had severe thyrotoxicosis. In the remaining 15 patients (24.2%), recurrence of the disease was observed two years after conservative treatment. Therefore, these patients underwent **total strumectomy**.

Table 1. Distribution of patients by age groups

Age group	Men (n=20)		Women (n=42)	
	number of observations %	number of observations %	numberof observations %	%
Up to 20 years	-	-	-	%
21-30 years old	-	-	-	-
31-40 years old	15	75,0	27	64,3
41-50 years old	5	25,0	15	35,7
51-60 years old	-	-	-	-
Over 61 years old	-	-	-	-

Note: *n* – number of patients examined.

Table 2. Characteristics of postoperative complications in patients of the recurrence group

Groups	1	2	3	4	5	6
Recurrence group (n=15)	15.0	2	3	1	4	-
	100%	13.3%	25.0%	6.7%	26.6%	0%
Total	15.0	2	3	1	4	-
	100%	13.3%	25.0%	6.7%	26.6%	0%

Note: p-reliability criterion, where values are given in comparison with the control

Table 3. Immunohormonal parameters of patients with diffuse toxic goiter before conservative treatment

By degree of thyrotoxicosis	T3 (1.6 ±0.01 nmol/L)	T4 (114,3±0,4 nmol/L)	TTG (1.6 ±0.19 mM/L)	Antibodies to rTTG (31.4 ±2.3 mE/ml)
Light degree n=19	3,04 ±0,01 ***	192,5 ±1,0 ***	1,5 ±0,4	231,79 ±12,80 ***
Average degree n=28	3,38 ±0,04 ***	206,4 ±2,4 ***	0,13 ±0,00 ***	259,85 ±17,60 ***
Severe degree n=15.	3,04 ±0,11 ***	194,3 ±5,2 ***	0,15 ±0,01 ***	293,5 ±30,90 ***
Control n=20.				

Notes: • The significance of differences in the 2nd column and subsequent columns is indicated according to the **Student's t-test**: – $p < 0.70$; $p < 0.30$; $p < 0.10$; $p < 0.05$. • **Row 1** – compared with the healthy control group. • **Row 2** – compared with the healthy control group and Row 1. • **Row 3** – compared with the healthy control group, Row 1, and Row 2.

Table 4. Immunohormonal parameters of patients treated conservatively and surgically after 1 month

Thyrotoxicosis severity	T3 (1,6±0,01 nmol/L)	T4 (114,3±0,4 nmol/L)	TTG (2.6 ±0.39 μM/ml)	rTTG (1.4 ±0.3 mE/L)
After traditional treatment				
Control, n=20	1,6 ±0,01	1,6 ±0,01	1,6 ±0,01	1,6 ±0,01
Light degree, n=19	1,20 ±0,06 ***	109,6 ±8,8 ***	1,0 ±0,11 ***	249,3 ±17,8 ***
Average degree, n=28	1,27 ±0,08 ***	92,3 ±4,9 ***	0,58 ±0,10 ***	252,4 ±29,0 ***
Heavy degree, n=15	1,2 ±0,12 ***	92,7 ±8,0 ***	0,29 ±0,07 ***	265,6 ±57,6 ***
After complex treatment				
Recurrence group P=15	1,34 ±0,05 ***	86,8 ±8,0 ***	0,77 ±0,11 ***	75,0 ±7,2 ***

Table 2 presents the characteristics of postoperative complications in patients according to the clinical groups.

Postoperative hypothyroidism, 2 - laryngeal swelling and asphyxia, 3 - dysphonia (damage to the superior laryngeal nerve), 4 - dysphagia (damage to the recurrent nerve), 5 - hypothyroidism, 6 - wound suppuration.

After analyzing the results, it was found that following traditional treatment in the main group, remission was

achieved in **47 (75.4%)** patients, whereas after the use of a comprehensive conservative treatment method remission was achieved in **15 (26.2%)** patients.

Compared with patients in remission, the frequency of relapses decreased **1.6 times in the comparative group ($p < 0.05$)** and **2.9 times in the main group ($p < 0.0001$)**. Thus, the addition of comprehensive treatment not only increased the number of patients who achieved remission but also reduced the frequency of disease recurrence.

Table 3 presents the immunohormonal parameters of patients with diffuse toxic goiter (DTG) before conservative treatment.

Analysis of the data presented in **Table 3** shows that the most pronounced immunohormonal disturbances were observed in patients with severe thyrotoxicosis. This group consisted of patients with disease recurrence during conservative treatment who subsequently underwent surgical treatment. The mean values of antibodies to TSH receptors (TRAb) significantly decreased as the severity of thyrotoxicosis increased.

Table 4 presents the immunohormonal parameters of patients treated conservatively and surgically after **one month**.

Analysis of **Table 4** shows that in patients of the recurrence group, during the postoperative period one month after total strumectomy, as well as in patients of the conservative treatment group, compensation of the condition and the development of postoperative hypothyroidism were observed.

Thus, changes in the titers of antibodies to TSH receptors (TRAb) during treatment may be useful for predicting recurrence after treatment with antithyroid drugs in patients who had positive thyroid peroxidase antibodies (TPOAb) at the time of diagnosis. The mean levels of antibodies to TSH receptors significantly decreased as the severity of thyrotoxicosis increased.

4. Conclusions

After traditional treatment in the main group, remission was achieved in **47 (75.4%)** patients, whereas after the use of a comprehensive conservative treatment method remission was achieved in **15 (26.2%)** patients.

Changes in the titers of antibodies to TSH receptors during treatment may be useful for predicting recurrence after antithyroid drug therapy in patients who had positive thyroid peroxidase antibodies at the time of diagnosis.

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