Health Quality Assessment of Patients with Toxic-Diffuse Goiter

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Abstract

In recent decades, there has been a significant increase in the number of patients with thyroid disorders[1,4]. The widespread introduction of highly informative diagnostics method (ultrasound, fine-needle aspiration biopsy, tests on hormones and levels of antibody) and screening studies into medical practice led to an increase in detection rate of thyroid disorders[4,5,8]. Among patients with thyroid pathology, the thyrotoxicosis syndrome significantly complicates the course of thyroid disorders, which makes it difficult to choose a rational treatment strategy, affects the long-term result of treatment, and significantly worsens the disease prognosis[8,10].

Keywords: *Thyroid disorders, Graves' disease, goiter, patient, grave.*

Introduction

In clinical practice, it is appropriate to distinguish 3 main diseases that occur with thyrotoxicosis syndrome: toxic diffuse goiter (Graves' disease), multinodular toxic goiter (MTG), and toxic adenoma (TA) of the thyroid gland. The surgeons most often face such disorders. In more rare cases, the cause of thyrotoxicosis development is iodine-induced thyrotoxicosis and inflammatory thyroid disorders - thyroiditis[8]. The thyroid disorders with thyrotoxicosis syndrome have characteristics of serious thyrotoxicosis complications that significantly worsen the course of the disease and its prognosis and influence the quality of life, such as endocrine ophthalmopathy, cardiomyopathy, arrhythmia, heart failure, weight loss, heat intolerance, insomnia, muscle weakness, pretibial myxedema, women often have menstrual disorders, men – gynecomastia, decreased libido, erectile dysfunction [1]. In case of Graves' disease, the endocrine ophthalmopathy (EOP) develops in 25-70% of cases[3], pretibial myxedema – in 2%[1]. In 5-22% of all cases the thyrotoxicosis syndrome occurs with cardiomyopathy, especially among elderly people that suffer from MTG[8]. The toxic diffuse goiter is a disease with such characteristics as increased production of thyroid hormones and diffuse growth of the thyroid gland (TG) of various degrees. The Graves' disease incidence varies from 30 to 200 per 100 thousand people within the course of one year. In regions with normal iodine supply, Graves' disease is the most common cause of persistent thyrotoxic condition, and in iodine-deficient regions, Graves' disease competes with the functional autonomy of the thyroid gland (nodular and multinodular toxic goiter) within the etiological structure of Graves' disease toxic goiter [4]. Graves' disease is one of the main causes of the endocrinological help request among population, it includes 80% of all thyroid hyperfunction cases and is most common in the age of 20 to 40 years; the disorders rate among women is in 10-20 times larger. The presence of symptoms that complicate the course of the disease undoubtedly negatively influence the health, performance and quality of life of patients [11]. In accordance with the evidence-based medicine, the study of the quality of life (QOL) among patients is mandatory in order to determine the efficiency of the treatment method [2]. The key treatment method of thyroid disorders with thyrotoxicosis syndrome ca n be combined into three groups: complex medicamentous therapy, radiotherapy (RT) and surgical treatment, used

separately and in various combinations. Each method has both advantages and disadvantages, which is a wide topic for discussion in the literature[12]. The standards of patients management with thyrotoxicosis (in accordance with the Russian, American, European, Chinese, Korean, Japanese, Australian, Latin American thyroid associations) differ significantly [13]. QOL (quality of life) is an indicator of a patient's physical, psychological, emotional and social functioning on the basis of their subjective condition perception[14].

The purpose of the research: To study the degree of toxic diffuse goiter incidence among thyroid pathologies and assess the quality of life among urban population of Urgench (Khorezm region, Uzbekistan) on the basis of the received therapy.

Materials and Method

The study included patients with thyroid pathology who sought medical service of endocrinological dispensary in Urgench from 2014 to 2019. We analyzed the medical history of 697 patients with thyroid pathology retrospectively. All patients passed the complete physical examination: General Clinical researches; hormones level detection (total T3, SV. T4, TSH); immunological indicators examination (Ab-r TSH,Ab-TPO). In addition to hormonal research, there was an ultrasound examination of the thyroid gland. There were scintigraphy and fine-needle biopsy of the thyroid gland among patients with nodules (by indications). We examined the timely visits of patients to endocrinologists, assigned standard therapy of toxic diffuse goiter. In order to study the quality of life among patients with Graves' disease, we used the SF-36 quality of life questionnaire, which reflects patients 'satisfaction with their physical and mental condition, social functioning, and self-assessment of the pain syndrom severity. We determined the sum of total score by 8 parameters: physical functioning, role functioning, pain intensity, general medical condition, vitality, social functioning, emotional functioning, and psychological health. The questionnaire has such design that a higher score reflects a higher level of quality of life. In addition, 20 healthy volunteers also completed a questionnaire to obtain benchmark indicators specific to healthy individuals. This questionnaire has Uzbek translation, and the patients managed to answer all the questions by themselves.

We used the quantitative assessment in regard to the following indicators: PF – physical functioning which reflects the extent to which the health state limits the performance of physical loads such as self-care, walking, stair climbing, heavy loads handling, body bending, and significant effort tolerance; RP is the influence of physical state on the role functioning (work, daily activities); BP – bodily pain and its impact on the ability to engage in daily activities like household duties inside and outside of the house; GH – general medical condition – health condition assessment by the patient at the moment and the prospects of a cure, resistance to disease; VT – vitality, a rise of vitality means feeling full of energy or, on the contrary, weakened; SF – social functioning, determined by the degree to which physical or emotional condition restricts social activities (communication); RE – influence of emotional state on role functioning, seeks to assess the extent to which emotional state interfere with work or other regular daily activities, as well as a heavy timetable, descrease of workload and its quality; MH – characteristics of mental health (depression, anxiety, general indicator of positive emotions).

The research materials were subject to statistical processing by means of statistics software packages Excel 2003, STATISTICA 6.0 (Stat-Soft, 2001).

Research Results and their Discussion

Table 1: The number of patients with thyroid cancer who applied to the endocrinological dispensary in the city of Urgench.

№	Nosology	Quantity
1.	Toxic diffuse goiter	109
2.	Diffuse-nodular goiter	24
3.	Toxic adenoma	45
4.	Diffuse goiter with euthyroidism	136
5.	Nodular goiter with euthyroidism	98
6.	Diffuse-nodular goiter with euthyroidism	72
7.	Autoimmune tireodit of thyrotoxic phase	23
8.	Autoimmune thyroidit with euthyroidism	79
9.	Condition after strumectomy	66
10.	Cysts of the thyroid gland	44
11.	Thyroid cancer	1

We examined the medical history of 697 patients with thyroid pathology. Among them there were 453 women and 244 men within the age range from 18 and

65. The duration of the disease with thyrotoxicosis was on the average of 8.3±2.1 years. The analysis of the patient's medical history revealed 109 (15.63%)patients with (Graves' disease), diffuse-nodular goiter among 24 (3.4%), toxic adenoma among 45 (6.48%), diffuse goiter with euthyroidism among 136 (19.51%), nodular goiter with euthyroidism among 98 (14.1%), diffuse-nodular goiter with euthyroidism among 72 (10.3%), autoimmune thyroiditis (AT) thyrotoxic phase among 23 (3.3%), AT euthyroidism among 79 (11.33%), condition after strumectomy among 66 (9.5%), thyroid cysts among 44 (6.31%), thyroid cancer in case of 1 (0.14%) patient (table 1).

The examination of the patient's medical history revealed that 178 (25.5%) patients within the group of the examined patients had thyrotoxicosis syndrome. We verified the thyrotoxicosis syndrome by the determination of thyroid hormones. The patients with Graves' disease had the average level of TSH around 0.1±0.02 MED/l, SV. T3-7,8±1.1 PG/ml, SV. T4-22.6±2.4 PG/ml, antibodies in relation to TSH receptors 2.3±1.2 IU/l, antibodies in relation to thyroperoxidase (TPO) - 58.7±3.1 IU/l (table.2.) Whereby, the reference values for TSH were 0.3-4.5 MED/l,for SV. T3 2.0-4.2 PG/ml, for ESV.T4-8,9-17,2 PG/ml, antibodies in relation to TPO-0-30ME/l, antibodies in relation to TSH receptors 0-1,49 IU/l.

Table 2: Changes in thyroid hormones in accordance with the pathology

Nosology of TG pathology	Control group, n=20	Graves ' disease, n= 109	Diffuse-nodular goiter, n= 24	Toxic adenoma, n=45
TSH, mU/l	2,2±0,7	0,1±0,02*	0,1±0,05*	0,1±0,02*
SV. T3, pg/ml	0,8±0,3	7,8±1,1*	6,2±1,3*	6,5±1,6*
Sv. T4, pg/ml	14,2±0,9	26,7±0,3*	29,4±0,4*	23,4±0,3*
Antibodies to TSH receptors, IU/l	0,3±0,02	3,4±0,5*	2,5±0,1*	2,9±0,5*
Antibodies to thyreoperoxidase, IU/l	20,6±3,4	58,7±3,1*	24,3±2,1*	27,7±2,7*

Note: Statistical significance to CG: * P<0.05 in relation to CG.

In case of endocrine profile interpretation, we found indications among 109 patients with Graves' disease, among them there were 72 (66 %) of female patients, and 37 (34 %) of male patients.

We diagnosed diffuse enlargement of the thyroid gland (TG) with palpation among each patient with Graves' disease in accordance with O. V. Nikolayev. We used the ultrasound examination in order to determine the volume and structure of the thyroid gland. We observed an TG increase of the 1st degree among 23 (21.1%) patients, of the 2 degree among 54 (49.5%), of the 3 degrees among 27 (24.8 %), of the 4 and 5 degrees among 5 (4.6%) patients. The ultrasound examination determined the volume of TG, with an average volume of 24.8±7.3 cm^3 among women and 32.3±9.3 cm^3among men.

By utilisation of services, we divided all patients with Graves' disease into 4 groups in accordance with the duration of the disease. The group 1 included patients with duration of the disease of up to 6 months, the group 2 up to 12 months and more than a year, the group 3 –3-5 years and the group 4 more than 5 years.

Table. 3: The complications development among patients with Graves' disease in accordance with the disease duration

Groups	Goiter heart	Endocrine ophthalmopathy	Toxic hepatitis	TSH, mU/l
1 group, n= 62	2 (3,2%)	24 (38,7%)	-	0,3±0,01
2 group, n=74	5 (6,8%)	32 (43,2%)	1(1,4%)	0,2±0,02
3 group, n=41	6 (14,6%)	26(63,4%)	2 (4,8%)	0,3±0,01
4 group, n=28	5 (18%)	19 (67,8%)	2 (7,1%)	0,4±0,01

In group 1, there were 62 patients who received thyrostatics with a daily dose of 25.4±2.1 mg/day (average TSH level of 0.3±0.01 Med/l), in group 2, 74 patients (thyrostatics with a dose of 20.3±2.4 mg/day and an average TSH level of 0.2±0.01 Med/l), in group 3, 41 patients that use of thyrostatics with a daily dose of 15.1±1.6 mg/day (average TSH level of 0.3±0.01 Med/l), in group 4, 28 patients that used thyrostatics with a daily dose of 12.2±1.1 mg on average (average TSH level 0.4±0.01 MED/l).As you can see, with the duration of the disease, there is a decrease in the dose of thyrostatics, but whereby there is no clinical improvement. The patients with Graves' disease with a duration of up to 6 months: we observed clinical and biochemical remission among 23 (37%) patients. The patients with Graves' disease with a duration of up to the 1st year: we observed clinical and biochemical remission among 34 (46 %) patients, in group 3 among 8 (19.5 %) patients and in group 4 - among 9 (32.1%) patients. The average TSH level was 1.2±0.05 med/l. we observed such complications as goiter heart among 2 (3.2%) patients, endocrine ophthalmopathy among 24 (38.7%) patients in the group 1, in group 2 among 5 (6.8%) patients, among 32 (43.2 %); in group 3 among 6 (14.6%), among 26 (63.4%);in group 4 among 5 (18%) and 19 (67.8%) patients, respectively. (table 3.). We did not detect any toxic hepatitis within the first group, there was 1.4% in group 2, 4.8% in group 3, and 7.1% in group 4 (table 3.) Within the examination of patients in these groups in relation to the treatment of Graves' disease, we observed that in group 1, 28 (45.1%) of patients showed improvement in their condition, 34 (54.9%) patients continued treatment with thyrostatics, despite the fact that there were indications for surgical treatment. In group 2, 24 (32.4%) patients recovered, 37 (50.0%) continued medication, and 13(17.6%) patients passed surgical treatment - total thyroidectomy. Among 24 recovered patients, the indicator of antibodies in relation to TSH receptors was on the average of 0.76±0.03 IU/l, respectively, these patients did not have clinical implications of thyrotoxicosis. In case of group 3 analysis, we observed recovery among 2 (4.9%) patients, respectively, the average level of antibody in relation to TSH receptors was 0.96±0.07 IU/l, 29 (70.7%) then the patients continued medication,since they had a high indicator of 2.3±0.05 IU/l that refer to the disorder persistence, and 12 (24.4%) passed operations. In group 4, 2 of patients (7.2 %) there was a health improvement (the average TSH level of 1.6±0.02 Med/l and TSH receptor in relation to antibodies by 0.72±0.02 IU/l), and 22 (78.6%) continued treatment with thyrostatics (average TSH level of 0.2±0.04 Med/l and TSH receptor in relation to antibodies by 2.5±0.09 IU/l) and 4 (14.3%) of patients passed medical operations(table.4.) The patients who had complaints with characteristics of the clinical thyrotoxicosis and the value of antibodies in relation to TSH receptors higher than the reference values, continued to take antithyroid medicines.

We should note that not all patients within the dynamics of treatment passed the examination on antibodies in relation to TSH receptors, since we indicated the start of disorder remission by the absence of thyrotoxicosis symptoms and normalization of antibodies in relation to TSH receptors and hormone indicators within the scope of thyroostatic therapy.

Table. 4: Dynamic observation of patients with toxic diffuse goiter

Group of patients	Recovered, n (%)	Prolonged medical treatment, n (%)	Surgical management, n(%)
1 group, n= 62	28 (45,1%)	34 (50%)	-
2 group, n= 74	24 (32,4%)	37 (50,0%)	13 (17,6%)
3 group, n= 41	2 (4,9%)	29 (70,7%)	12 (24,4%)
4 group, n= 28	2 (7,2 %)	22 (78,6 %)	4 (14,3 %)

The diffuse-nodular goiter within the TG pathology constituted 24 (3.4%) patients, and toxic adenoma 45 (6.45%) patients. During palpation and ultrasound examination, we found nodes up to 1 cm among 26 (37.7%) patients, and more than 1 cm among 43 (62.3%) patients. We made the diagnosis by means of hormone testing and TG scintigraphy. We performed the scintigraphy in the RSPC of the endocrinology. We found inflammation spots by scintigraphy. All patients received the medicamentous therapy with thyrostatics

until subclinical hypothyroidism progress within 3-6 months and passed surgery operations.

In case of the conducted thyroostatic therapy analysis among patients with Graves' disease, we found that among them 28 (25.6%) patients received long-term medication for up to 10 years with inappropriate medicamentous therapy within the latest medicine doses in regard to the severity of thyrotoxicosis and it caused various complications of Graves' disease. Subsequently, in case of ineffective medicamentous therapy for more than 5 years, 20 (71.4%) patients had a thyroidectomy, among them 9 (45.0%) patients had subtotal thyroidectomy and 11(55.0%) had total thyroidectomy. We performed the thyroidectomy in the department of surgery in the city endocrinological dispensary of Urgench. Within the treatment period from 3 to 5 years, 6 patients with cardiovascular complications did not referred for surgical treatment service and continued thyrostatics treatment. In case of operated patients observation within 3 and 6 months, we observed a decrease in the functional activity of the TG among 8 (27.6%) patients, since there was no prescription for timely hormone replacement therapy (HRT) with thyroid medications. Among the operated patients, only 5 patients (17.2%) in the early postoperative period received HRT with levothyroxine at a dose of 1.2±0.5 mcg/kg per day without full compensation. In the study of TSH and SV. T4 patients we diagnosed subclinical hypothyroidism among these, with an average TSH level of 5.4±0.7 MED/l. In order to correct these disorders, we increased the dose of levothyroxine to 1.6 mcg/kg. Whereby, the average TSH level was 5.4±0.7 MED/l. 15 patients after thyroidectomy did not come for reexaminations. In accordance with the indications, if the patient refuses surgical treatment, there were recommendations in regard to 2 patients to pass treatment with radioactive iodine in the radiological Department in the RSPC of the endocrinology.

In addition, we diagnosed T3 toxicosis among 2 women, whereby both had a common fraction. In the medical history analysis of these women, we found that they used HRT for a long time together with sex hormones. On ultrasound examination of the thyroid gland, we diagnosed a diffuse goiter of 1-2 degrees without any structural changes of TG. It is known that the medication intake leads to an increase in total T3, whereby the content of total and SV. T4, as well as TSH stay within the norm[7]. Clinically, these women did not have any complaints. These women stopped HRT by sex hormones and they got a prescription to use other non-hormonal method of pregnancy prevention.

We used a QOL questionnaire SF-36 in order to study the quality of life among patients with Graves' disease on the basis of the received therapy. We divided all patients with Graves' disease into 2 groups. The first group included 30 patients with Graves' disease who had received medicamentous therapy for more than three years and the second group 24 patients after thyroidectomy in case of Graves' disease. Among 29 patients under surgery, 3 (10.3%) had hypoparathyroidism as postoperative complication, and 2 (6.9%) had recurrent nerve paresis. These patients visited an endocrinologist and an otorhinolaryngologist in order to pass rehabilitation. We did not include these patients into this group. Among the patients of both groups, all parameters of quality of life present with examination were significantly lower than among healthy individuals ($P<0.001$) by all scales of vitality within group 1: $P<0.01$ for the vitality scale in group 2 and $P<0.001$ for all other parameters in group 2. (table 5.). Between the patients of two groups there were the following differences: the parameters physical functioning, vitality, social, emotional functioning and mental health were significantly higher in the group of patients after total and subtotal thyroidectomy ($P<0.001$),the role functioning was not significantly different in both groups of patients, and indicators of social functioning were significantly higher (30.7%) in the group of patients under medicamentous therapy by thyreostatics($P<0.001$), as endocrine ophthalmopathy was more large in this group. Within the comparison of the QOL among patients with Graves' disease within both groups, we found that the average values of physical functioning, role-based physical functioning, social functioning , role- based emotional functioning and mental health after surgery significantly exceed similar indicators among patients who received medications with thyrostatics, although the average level of TSH in both groups did not significantly differ. In the first group, the average TSH level was 2.3±0.02 Med/l, in the second group 3.1±0.05 MED/l. The emotional functioning and psychological health in the 2 group of patients are higher by 40.7% and 22.5%, respectively.

Table 5: Parameters of QOL assesment among patients with Graves' disease in accordance with the treatment

Parameters	CG, n=20	1 group, n=30	2 group, n=24
Physical functioning	60,35±2,21	17,43±3,08***	22,33±5,38***^
Role functioning	64,52±3,28	24,10±3,24***	28,14±3,62***
Pain	12,16±3,74	20,13±1,41***	15,32±6,72***
General medical condition	58,17±3,26	45,23±2,33***	47,02±3,14
Vitality	78,06±2,76	30,50±2,11***	46,25±4,22**^
Social functioning	52,13±1,84	27,33±2,59***	39,95±3,02***
Emotional functioning	81,57±2,41	29,53±1,70***	49,81±2,97***^
Psychological health	74,65±2,57	48,27±1,95***	61,28±2,64^

Note: Statistical significance with CG: * * P<0.01, ***P<0.001; statistical significance between groups 1 and 2: ^P<0.05 CG-control group

Thus, the timely appointment for thyroidectomy in cases of Graves' disease in real time leads to patients health improvement. After thyroidectomy, all patients should pass a hormone examination in order to fulfill timely hormonal replacement therapy. Timely appointment for hormonal replacement therapy with thyroid medications improves the quality of life and prevents the development of complications within various organs and systems.

Conclusions

1. Among the examined patients of the Urgench endocrinological dispensary that suffered the thyroid pathology in 2014 - 2019,we observed:15.6% of toxic diffuse goiter, 3.4% of diffuse-nodular goiter, toxic adenoma in 6.4% cases, diffuse goiter with euthyroidism in 19.5% cases, nodular goiter with euthyroidism in 14% cases, mixed goiter with euthyroidism in 10.3% cases, autoimmune thyroiditis, thyrotoxic phase in 3.3% cases, autoimmune thyroiditis with hypothyroidism in 11.3% cases, condition after strumectomy in 9.5% cases, thyroid cysts in 6.31% cases, thyroid cancer in 0.14% cases.
2. The quantity of patients with toxic diffuse goiter and goiter heart was 3.2%, endocrine ophthalmopathy 38.7% of patients within the first group, within group 2 6.8% and 43.2 %; within group 3 in 4.6% and 63.4%; within group 4 in 18% and 67.8%, respectively. There was no diagnosis of toxic hepatitis within the first group, 1.4% within group 2, 4.8% within group 3, and 7.1% within group 4, respectively. We should note that with an increase in the duration of inadequate thyrostatic therapy, the percentage of these complications increases, which confirms the need for correct medicine management and a timely transition to radical method of treatment.
3. In case of ineffective medication, only 26.6% of patients had a thyroidectomy. After surgery, only 17.2% received HRT with levothyroxine at a dose of 1.2±0.5 mcg/wt per day without full compensation. The remaining 55.1% of patients did not come to reexaminations. In order to improve the diagnosis and treatment of thyrotoxicosis syndrome in the Khorezm region, we recommend to conduct a number of seminars for doctors.
4. In comparison between the QOL among patients with Graves' disease after timely thyroidectomy, the average values of physical functioning exceed by 23% in relation to medicamentous therapy, the indicators of emotional functioning and mental health, as well as social functioning significantly exceed by 40.7%, 22.5% and 30.7%, respectively, similar indicators of patients under medicamentous therapy with thyrostatics.
5. We observed hypoparathyroidism among 0.3% of patients with toxic diffuse goiter after total thyroidectomy and among 6.9% of patients with recurrent nerve paresis, which indicates the need for training of operating surgeons in Urgench at the workplace of experienced surgeons.

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