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# MARKAZIY OSIYO ENDOKRINOLOGIK JURNALI

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# INFLUENCE OF BARIATRIC SURGERY ON THE THYROID STATUS OF OBESITY PATIENTS

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**ABSTRACT**

The many health benefits of bariatric surgery are known, but there is limited data on the benefits of bariatric surgery on thyroid function. PubMed, Medscape, EMBASE, Cochrane Library, ScienceDirect, Elsevier, ResearchGate, Google Scholar were searched up to and including March 2024 for studies on the effects of bariatric surgery on thyroid hormone levels and postoperative levothyroxine dosage.

**Key words:** bariatric surgery, thyroid hormone, obesity, levothyroxine

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# СЕМИЗЛИГИ БОР БЕМОРЛАРДА БАРИАТРИК ЖАРРОХЛИКНИНГ ТИРЕОИД СТАТУСИГА ТАЪСИРИ

**АННОТАЦИЯ**

Бариатрик жаррохликнинг (БЖ) бир қанча фойдали томонлари етарлича ўрганилган, аммо, тиреоид функцияга таъсири ҳақида маълумотлар кам. PubMed, Medscape, EMBASE, Cochrane Library, ScienceDirect, Elsevier, ResearchGate, Google Scholar ва РИНЦ электрон базаларидаги 2024-йил март ойига қадар топилган илмий адабиётларда БЖ нинг амалиётдан кейинги даврда тиреоид гормонлар даражасига ва левотироксин дозасидаги ўзгаришларга таъсири кўриб чиқилди.

**Калит сўзлар**: бариатрик жаррохлик, тиреотроп гормон, семизлик, левотироксин.

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# ВЛИЯНИЕ БАРИАТРИЧЕСКОЙ ХИРУРГИИ НА ТИРЕОИДНЫЙ СТАТУС ПАЦИЕНТОВ С ОЖИРЕНИЕМ

**АННОТАЦИЯ**

Многие преимущества бариатрической хирургии для здоровья известны и хорошо изучены, но данных о пользе бариатрической хирургии для функции щитовидной железы недостаточно. В базе данных PubMed, Medscape, EMBASE, Кокрановской библиотеке, ScienceDirect, Elsevier, ResearchGate, Google Scholar за период до марта 2024 г. включительно был проведен поиск исследований влияния бариатрической хирургии на уровень тиреоидных гормонов и дозу левотироксина после перенесенной операции.

**Ключевые слова**: бариатрическая хирургия, гормоны щитовидной железы, ожирение, левотироксин.

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According to the World Health Organization, 650 million adults and more than 379 million children and adolescents are living with obesity worldwide by 2023 [3,44]. Obesity occurs in 11% of men and 15% of women in the world [36] and has become an epidemic problem for health organizations [37]. 20% of overweight patients in the USA are morbidly obese [22]. The increase in obesity-related diabetes and other metabolic syndrome diseases, and the increase in early morbidity due to age are one of the most urgent problems of today's modern medicine. In morbidly obese patients, lifestyle modification and drug therapy usually fail to achieve effective and sustainable weight loss [9]. Therefore, bariatric surgery (BS) is recognized as the most effective method for long-term weight loss and effective treatment of many metabolic disorders [17]. The greatest changes in weight loss are undoubtedly observed after BS [13]. High BMI (<35), hyperlipidemia, diabetes and hypertension independently increase the risk of death [41,42]. Studies have reported that the average life expectancy of obese people is reduced from 5 to 20 years [19]. Over the past 10 years, bariatric surgery has been spread all over the world and recognized as the most long-lasting treatment for obesity [16]. These practices seem to have solved the problem of obesity and its complications, resulting in high development and growth rates in many countries around the world [1]. Bariatric surgery (from Greek baros - heavy) is a surgical procedure performed on the organs of the digestive tract to reduce body weight [4]. According to the updated National Institutes of Health organizations criteria for BS, BMI >35 kg/m2 or 30-34.9 kg/m2 in patients with metabolic disease, BMI >25 kg/m2 is considered obesity for Asian populations, and BMI >27.5 kg/m2. m2 is an indication for BS [1,16].

Studies have shown that BS increases life expectancy by reducing the risk of death, and the implementation of BS in healthcare organizations may improve the future of morbidly obese patients [32]. The International Federation for Surgery of Obesity and Metabolic Disorders (IFSO) provides an annual report of bariatric procedures performed since 2014 based on pooled data from 51 countries [32,46]. According to the fourth IFSO Global Registry report 2018, the mean weight loss 1 year after intervention was 28.9%, and 66.1% of patients discontinued type 2 diabetes medications [46]. BS improves the metabolic status of the whole body through several physiologic mechanisms: decreased caloric absorption, changes in gut [31] and endocrine hormones [12], changes in neurohumoral control [39], changes in gut microflora, bile acid production, and many other factors determine that the next overall metabolic change will occur. However, many other effects and outcomes of BS practice are not yet fully understood [43]. The effects of BS on non-insulin-deficient diabetes, hypertension, and sleep apnea have been widely studied, but literature on its effects on thyroid function is lacking [26]. In particular, thyroid hormone is the most important controlling hormone in maintaining thermoregulation and energy balance of the body [20]. Several studies are known to have been conducted on the manifestation of thyroid hormone deficiency in weight gain. 54% of primary hypothyroidism patients complain of weight gain [6]. It was found that thyroid hormone imbalance, i.e., increased amount of TSH and increased conversion of free T4 to free T3, is more common in obese people [28]. Moreover, 11.8% of morbid obese patients have primary hypothyroidism and 7.7% of them have subclinical thyroid hormone (TSH) elevation [5]. In several observations, it was found that the post-operative decrease in adipokines, in particular leptin, is accompanied by a decrease in TSH, which in turn shows a positive correlation between TSH and body mass index (BMI) [7]. In follow-up analyses after bariatric procedures, decreases in serum TSH and free T3 were observed, as well as percent body weight loss in patients [27], which is thought to be related to changes in the

secretion of adipokines, especially in hormone of leptin [30,21]. Physiologically, leptin regulates energy homeostasis, informs the CNS about adipose tissue reserves [15,35], and influences neuroendocrine and behavioral responses to overeating, while TSH, in turn, stimulates leptin production in adipose tissue [29]. In obese patients, the mechanism of leptin activation of the satiety center is impaired and the sense of satiety in humans is reduced [8]. This, in turn, leads to a decrease in the activity of thyroid hormones and stimulation of thyroid hormone receptors, which subsequently causes an increase in TSH and free T3 in the blood [33,8]. Over the past 5 years, surgical treatment of obesity and a number of metabolic diseases has been widely used in Uzbekistan. Postoperative monitoring and treatment of nutrient deficiencies are widely established, but changes in thyroid hormone status has not fully understood yet. At the same time, the Republic of Uzbekistan is a region with long-term iodine deficiency, and this has a significant impact on thyroid status [2]. Therefore, it is necessary to study the influence of BS on thyroid function in iodine deficient regions. The results of several scientific studies the effect of BS on thyroid function are analyzed below.

A retrospective review of 93 patients (85 women, 91%) with hypothyroidism who underwent BS from 2010 to 2014 in the Department of Surgery at Chaim Sheba Medical Center in Israel, was performed. 83(89.2%) of them were receiving hormone replacement therapy. 77(82.8%) patients underwent VSG and 16 patients underwent Roux-en-Y gastric bypass (RYGB). The mean age and BMI of the patients were 46.6±11.2 years and 43.7±6.4 kg/m2 [50]. Basically, BMI and TSH decreased significantly after 6 and 12 months. Ziru Tian showed a reduction in TSH from 2.33(1.67, 3.04) uIU/mL to 1.82 (1.21, 2.50) uIU/ml ($P < 0.001$) in 256 obese patients with euthyroid thyroid status who underwent bariatric surgery from 2017 to 2022., Free T3 decreased from 3.23 ± 0.42 pg/ml to 2.89 ± g/0.41 (pg/0.41). Free T4 decreased months of surgery, and free T4(fT4) levels stabilized (Table 1) [45]. Scientists from China's Fudan University studied the functional status of the thyroid and its autoimmune status in 101 patients (44 males and 57 females, mean age 33.4, BMI-42.1 kg/m2) who underwent BS at Zhongshan Hospital from June 2014 to June 2017. Results were evaluated before and after. According to the results: Serum thyroperoxidase antibody (TPOAb) and (≥ 115 IU/mL) in 4 patients thyroglobulin antibody (TgAb) (≥ 34 IU/mL) in 5 patients. Serum thyroperoxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) levels also decreased significantly (from 79.3 and 177.1 IU/mL to 57.8 and 66.0 IU/mL). The changes in metabolic parameters and changes in TSH, fT4 are summarized in Table 1 [47].

Another retrospective study was conducted from 2010 to 2015 by scientists from the Faculty of Medicine of the University of Porto and the Department of Endocrinology at the Central Hospital of Portugal. They studied 949 (86.1% women; age 42.0±10.3 years, TVI 44.3±5.7 kg/m2) morbidly obese euthyroid patients who underwent bariatric surgery, divided into 2 groups according to TSH level. Accordingly, patients in the normal TSH (TSH<2.5 mU/L) and high-normal TSH (TSH≥2.5 mU/L) groups were compared to TSH changes 12 months after surgery, comorbidity, free T4, free T3, type of surgery and excess body mass. the effect of its loss was studied. According to the results, the majority of those in the high-normal-TSH group (24.3%) were women. A significant decrease in TSH levels was observed 12 months after surgery, with a significant change in the high-normal TSH group (normal TSH group: 1.57±0.49 to 1.53±0.69 mME/L, p=0.063; high-normal TSH group: from 3.23±0.59 to 2.38±0.86 mME/l, p<0.001). The conclusion was that BS helps to lower TSH and this is more pronounced in patients with high TSH levels. A decrease in TSH levels is independently associated with the loss of excess body mass after exercise [34]. Jingge Yang conducted a retrospective study examining thyroid functional status in euthyroid patients before BS and 12 months after the procedure. A correlation was found between weight loss and thyroid function (Table 1) [48]. Another study to determine the effect of bariatric procedures on the thyroid status of hypothyroid patients was conducted by Yaron Rudnicki from 2011 to 2016 at the Department of Surgery, Meir Medical Center, Tel Aviv University, Kfar Saba, Israel. Of 1756 BS patients, 90 (5.1%) had a diagnosis of hypothyroidism, and 79 of them received hormone replacement therapy. The average daily dose at baseline was 114 mcg (25-500 mcg/day). 79 patients were monitored for changes in TSH and daily levothyroxine exposure for 11±9.73 months after surgery [40]. Dickson Dewantoro and his team divided 57 patients with hypothyroidism into 2 groups and observed them. 38 of them

underwent surgery, the remaining 19 did not undergo BS and were included in the control group (out of 57 patients, 50 (87.7%) were women, average age 47.26+/- 8.89, TVI 48.72+/-8.68 kg/m2 LT4 dose was initially 115.8+/- 53.5 mcg in the control group, 149.8+/- 68.4 mcg in the surgical group). 22 of the patients who underwent VSG, 16 underwent malabsorptive surgery. According to the results: There was no significant difference in the LT4 dose in the patients in the surgical group and the control group at 12, 24, 36 months of follow-up (p=0.67). When comparing surgical group patients into restrictive and malabsorptive groups, patients in the VSG group received 23.57 mkg less LT4 than those in the malabsorptive group (p=0.033) [14]. Groups of scientists led by Jan Peter Yska [49], Ming-Feng Xi [47], Helena Julia [25], Alex Zendel [50] studied changes in thyroid replacement therapy in patients who underwent BS. Their study included follow-up 2-4 years after surgery. Tables 1 and 2 below show the changes in BMI, TSH, fT4, daily dose of levothyroxine after surgery.

Table 1. Metabolic changes and thyroid hormone patterns before and after BS.

| Author | Number of patients | Follow-up period in month | Mean age | BMI (kg/m2) Before BS | BMI ( kg/m2) after BS | TSH mIU/L at baseline | TSH mIU/L after | fT4 pmol/l at baseline | fT4 pmol/l after BS |
|---|---|---|---|---|---|---|---|---|---|
| Zendel A | 93 | 6 m | 46.6 ± 11.2 | 43.7± 6.4 | 34.4±5.6 | 3.9± 2.8 | 3±2.7 | 13.7± 3.1 | 15±4.2 |
| Xia M | 101 | 12 m | 33.4 | 42.1 ± 7.6 | 31.4 ± 6.5 | 4.94± 3.13 | 4.33 ± 2.26 | - | - |
| Tian Z | 256 | 12 m | 35.00 | 38.37 ± 7.24 | 28.77± | 2.33 | 1,82 | 14.28 ± 3.217 | 13,12± 3,2 |
| Neves J | 949 | 12 m | 42.0 ± 10.3 | 44.3± 5.7 | 31.11± 5.38 | 3,23± 0,59 | 2,38 ± 0,86 | 13.38 ± 1.67 | 13.51± 1.67 |
| Yang J | 16 | 12 m | 35.7 | 35,78 | 23,66 | 2,31 | 1,54 | 15,19 ± 0,33 | 14,85± 0,85 |
| Yska J | 37 | 12 m | 47±10 | 44.2± 5.3 | 30.6 ± 4.6 | 1.77 (1.14–2.78) | 1.31 (0.89 – 2.82) | - | - |
| Julia H | 35 | 24 m | 45.2 ± 9.9 | 42 ± 4.4 | 32.5± 5.21 | 3.08 (0.51–4.79) | 2.82 (1.17 – 4.76) | 17.76 ± 3.08 | 22.2 ± 3.62 |
| Rudnicki Y | 79 | 11 m | - | 43.8 | 33.2 | 6.6±1.9 | 2.9± 1.5 | - | - |
| Dewantoro D | 57 | 12 m | 47.26± 8.89 | 48.72± 8.68 | 36.8± 4.8 | 4.2 (0.52-3.5) | 2.6 (1.08 - 3.92) | - | - |

However, levothyroxine is the main substance in the treatment of hypothyroidism [24], and 60% to 80% of the active substance is absorbed in the small intestine and duodenum of a healthy person [23]. There are reports in the literature of impaired absorption of levothyroxine after BS (both gastric bypass by Ru and VSG) [33], its absorption occurs predominantly in the small intestine and upper ileum and varies depending on gastric pH, other drugs, food, and other factors. Increases in

TSH and LT4 after BS have also been reported in several patients with hypothyroidism [18]. We analyzed 9 articles devoted to the functional status of the thyroid after BS, and 6 of them were devoted to the observation of postoperative changes in the daily dose of LT4. We studied thyroid status of 373 obese patients receiving hormone replacement therapy after BS (Table 1).

Change in lT4 dose after surgery. Table 2

| Authors | Number of patients | Follow-up period (in month) | Changes in daily dosage of LT4 after BS | |
|---|---|---|---|---|
| | | | reduced | Not changed |
| Zendel A., 2017 [50] | 83 | 48 | 11 | 72 |
| Yska J.P., 2022 [49] | 37 | 48 | 7 | 23 |
| Rudnicki Y., 2018 [40] | 79 | 24 | 13 | 22 |
| Julia H., 2019 [25] | 35 | 60 | 8 | 5 |
| Xia M. F., 2019 [47] | 101 | 36 | 3 | 6 |
| Dewantoro D., 2022 [14] | 38 | 36 | 0 | 57 |

Researchers led by Carmil Azran conducted a comprehensive meta-analysis at 2021 Herzliya Medical Center in Israel. This analysis reviewed 28 studies involving 1,284 patients examining the effect of bariatric surgery on TSH levels, levothyroxine dose, and subclinical hypothyroidism status. The researchers analyzed clinical trials on this topic through December 2020 in PubMed, EMBASE, and the Cochrane Library. According to the results, there was a statistically significant decrease in TSH levels after bariatric surgery (mean difference = -1.66 mU/dL, 95% CI (-2.29, -1.03, $P < 0.0001$). A meta-analytic study showed that in follow-up studies, mean age, baseline TSH levels, and postoperative thyroid function were 1%, 43%, and 88%, respectively [10]. In addition, 87% of patients with subclinical hypothyroidism receiving levothyroxine had a statistically significant reduction in daily hormone replacement therapy (difference in therapy doses = -13.20 mcg/d, 95%CI -19.69, -6.71) [11].

Most of the studies reviewed above showed that morbidly obese patients without thyroid disease had elevated serum TSH levels before bariatric surgery and postoperative weight loss helped to reduce TSH levels. However, some sources report that the postoperative decline in TSH is progressive [38], while others estimate the decline to be only up to 2 years. Some studies have focused on the effect of weight loss on TSH alone. In conclusion, according to the results of this meta-analysis, BS is a comprehensive solution to reduce subclinical hypothyroidism, daily levothyroxine dose and TSH levels. However, changes in thyroid function after BS in iodine-deficient areas are not fully understood and require long-term follow-up.

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