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Effectiveness of Bariatric Surgery for Improving Thyroid Function and Reducing Levothyroxine Dose in Patients With Obesity and Overt Hypothyroidism

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Abstract

Background: Hypothyroidism is a major hormonal condition that affects more women than men in Saudi Arabia. Studies indicate a bidirectional link between hypothyroidism and obesity, which may improve following bariatric surgery (BS). The focus of this research is to assess how hypothyroidism patients' thyroid function and levothyroxine dosage are impacted by bariatric surgery.

Methodology: This was an observational retrospective study conducted in two centres at Taif, Saudi Arabia. All morbidly obese patients who were diagnosed with overt hypothyroidism and underwent laparoscopic sleeve gastrectomy from January 2016 to December 2021 were included. The changes in the thyroid profile and the changes in the doses or cessation of levothyroxine were evaluated after the laparoscopic sleeve gastrectomy.

Results: Our results demonstrate that a total of 70 patients dominated by women out of 1202 from both centers who meet our inclusion criteria showed a statistically significant decrease on comparison of clinical parameters (thyroid-stimulating hormone [TSH], free T4 [FT4], free T3 [FT3], levothyroxine [L-T4]) before and after BS. The average TSH levels were determined to be 4.45 ± 4.41 mIU/L prior to BS, and they significantly decreased (3.17 ± 2.77 mIU/L) following BS (p=0.009). When compared to before BS (13.17 ± 2.73 pmol/L), the mean FT4 levels after BS (11.63 ± 5.88 pmol/L) exhibited a significant decline (p=0.046). The mean FT3 levels before and after BS also were statistically significantly lower (1.94 ± 2.12 pg/mL) than before (2.75 ± 1.96 pg/mL), p=0.009. The mean L-T4 levels after BS considerably decreased from before BS (98.68 ± 56.18 mcg) to after BS (79.39 ± 41.49 mcg), p=0.046.

Conclusion: Better thyroid profiles and lower levothyroxine dosage show that bariatric surgery improves hypothyroidism.

Categories: General Surgery
Keywords: sleeve gastrectomy, levo-thyroxine treatment, hypothyroidism, obesity, bariatric surgeries

Introduction

The thyroid gland is a highly vascular endocrine gland responsible for several vital processes in the human body, including metabolism, growth, and development, which are regulated by triiodothyronine (T3) and thyroxine (T4) [1]. Primary overt hypothyroidism is characterized by insufficient synthesis of T3 and T4, accompanied by an increased serum thyroid stimulating hormone (TSH) level [2]. Hypothyroidism can affect the functionality of several organs and tissues, and its signs and symptoms range from minor to life-threatening, depending on the severity of the hormone deficit. Early detection of hypothyroidism can be achieved through a thyroid function test that evaluates hormone levels. The only medication proven to effectively treat primary overt hypothyroidism is levothyroxine (L-T4) [3].

Hypothyroidism is more commonly observed in Saudi women than men, consistent with its higher global prevalence among women. A recent hospital-based study conducted in Jeddah, Saudi Arabia, reported a hypothyroidism prevalence of 29.1% among 3,872 participants, the majority (85.7%) of whom were female [4-6]. Obesity is a significant threat to public health, as it is a leading cause of many life-threatening diseases and conditions including hormonal abnormalities in the thyroid glands [7]. There is strong evidence of a bidirectional relationship between obesity and thyroid dysfunction [8]. Weight gain is a common symptom of hypothyroidism, which accordingly has a relatively high incidence among individuals with obesity. Thyroid hormones play a role in regulating the metabolic rate. A systematic review and meta-analysis conducted in 2019 confirmed that obesity is a risk factor for overt hypothyroidism [9,10]. Furthermore, several studies have indicated that individuals with obesity have a 70% increased risk of developing subclinical hypothyroidism [8,11].

Bariatric surgery (BS) is a weight-reduction surgery that involves multiple procedures designed to restrict the ability of the body to ingest and absorb food, by decreasing stomach capacity or intestinal length [12]. In 2016, Al-Khaldi [13] reported that approximately 15,000 BS are performed annually in Saudi Arabia. The three main types of BS are restrictive, malabsorptive, and both in combination [14]. Restrictive surgery involves removing and narrowing the stomach with laparoscopic sleeve gastrectomy (LSG); this accounts for half of all bariatric procedures performed globally [15]. Laparoscopic Roux-en-Y gastric bypass is a combination of restrictive and malabsorptive surgery that accounts for 30% of all bariatric procedures. Additionally, less frequently performed procedures included duodenal switch (DS), single-anastomosis duodeno-ileal bypass (SADI), and one-anastomosis gastric bypass (OAGB) [14,15]. The Saudi Arabian Society for Metabolic and Bariatric Surgery has established inclusion criteria for BS, which include an age of 14-65 years, body mass index (BMI) of ⩾ 35 kg/m2 (or ⩾ 30 kg/m2 if there are associated comorbidities), and failure to achieve weight loss through nonsurgical methods [16]. Several studies have demonstrated improvements in the thyroid profile following BS in obese patients [17-19].

Few studies have evaluated the effect of BS on hypothyroidism in Saudi Arabia, and no studies have been conducted in the Taif province. This study aimed to evaluate the ability of BS to improve overt hypothyroidism.

Materials And Methods

A retrospective observational study was conducted at two main hospitals in Taif, Saudi Arabia. Data of patients who underwent LSG or Roux-en-Y gastric bypass and were diagnosed with hypothyroidism between 2016 and 2021 were extracted from the hospital database. In total, 70 of 1,202 patients met the study inclusion criteria. The patients were required to have a body mass index (BMI) ⩾ 40 kg/m2 (or ⩾ 35 kg/m2 if associated with comorbidities such as hypertension, diabetes, hyperlipidemia, and obstructive sleep apnea). Hypothyroidism was diagnosed by an endocrinologist or family physician during two or more preoperative visits. The patients had no history of other thyroid diseases, such as tumors or surgery. Patients who were lost to follow-up were excluded from the study.

The preoperative data extracted from the medical records were baseline demographic information, BMI, L-T4 doses, and serum levels of TSH, free T4 (FT4), and free T3 (FT3). Overt hypothyroidism was diagnosed in patients who received L-T4 treatment and had elevated TSH and reduced T4 levels. Subclinical hypothyroidism was diagnosed in patients who had not received L-T4, and had elevated TSH and normal T4 levels. The final postoperative visits to surgery, endocrinology, and family medicine clinics, as well as the thyroid hormone levels and L-T4 doses, were recorded. The normalization of thyroid hormone levels after L-T4 administration indicated resolution of overt hypothyroidism, whereas a decrease in the L-T4 dose was considered to denote improvement, and no dose change indicated no improvement.

Statistical analysis was performed using SPSS software (version 23.0; IBM Corp., Armonk, NY, USA). Descriptive analysis was performed for categorical data, and the results are presented as frequencies and percentages. Tables and figures summarizing the data are presented. The Shapiro-Wilk test was used to determine the normality of the data distribution. Mean and standard deviation values were calculated for normally distributed data, whereas the median and interquartile range were calculated for non-normally distributed data. Continuous and categorical variables were compared using Student's t-test or the Mann-Whitney U test, as appropriate. P-values < 0.05 were considered statistically significant. The study protocol was approved by the institutional review boards of both hospitals.

Results

We evaluated the effect of BS on thyroid function by analyzing clinical parameters, including L-T4 doses and serum levels of TSH, FT4, and FT3. The analysis was based on the availability of data on each clinical parameter in the patients' medical records. The mean TSH level before BS was 4.45 ± 4.41 mIU/L, which was significantly reduced after BS to 3.17 ± 2.77 mIU/L (p = 0.009). The mean FT4 level after BS (11.63 ± 5.88 pmol/L) was significantly lower than before BS (13.17 ± 2.73 pmol/L) (p = 0.046). A statistically significant reduction was observed in the mean FT3 level, from 2.75 ± 1.96 pg/mL before BS to 1.94 ± 2.12 pg/mL thereafter (p = 0.009). Moreover, the mean L-T4 dose administered after BS was significantly lower (79.39 ± 41.49 mcg) than that before BS (98.68 ± 56.18 mcg) (p = 0.046) (Table *1*).

		N(%)	Mean	Std. Deviation	p value*
TSH	Pre TSH	66(94)	4.45	4.41	0.009
	Post TSH	66(94)	3.17	2.77	
FT4	Pre FT4	62(89)	13.17	2.73	0.046
	Post FT4	62(89)	11.63	5.88	
FT3	Pre FT3	35(50)	2.75	1.96	0.009
	Post FT3	35(50)	1.94	2.12	
L-T4 (mcg)	Pre L-T4	57(81)	98.68	56.18	0.046
	Post L-T4	57(81)	79.39	41.49	

TABLE 1: Comparison of clinical parameters before and after

TSH: thyroid-stimulating hormone, FT4: free T4, FT3, free T3, L-T4: levothyroxine

When comparing the mean TSH level before and after BS separately in females and males, we found no statistically significant differences (p = 0.056 and p = 0.065, respectively). Similarly, the mean FT4 level did not show statistically significant differences after BS in females (p = 0.066) or males (p = 0.323). However, we observed a significant reduction in the mean FT3 level after BS in females (p = 0.014), but not in males (p = 0.500). In addition, a statistically significant reduction in the mean L-T4 dose administered after BS was observed in females (p = 0.001) compared to males (p = 0.0197), as shown in Table 2.

Gender			N(%)	Mean	SD	P value*
Female	TSH	Pre TSH	59(84)	3.85	2.80	0.056
		Post TSH	59(84)	2.97	2.30	
	FT4	Pre FT4	55(79)	13.12	2.73	0.066
		Post FT4	55(79)	11.55	6.20	
	FT3	Pre FT3	33(47)	2.78	1.93	0.014
		Post FT3	33(47)	2.05	2.13	
	L-T4 mcg	Pre L-T4 mcg	50(71)	94.50	56.76	0.001
		Post L-T4 mcg	50(71)	76.00	42.55	
Male	TSH	Pre TSH	7(10)	9.46	10.11	0.065
		Post TSH	7(10)	4.86	5.32	
	FT4	Pre FT4	7(10)	13.61	2.90	0.323
		Post FT4	7(10)	12.32	2.29	
	FT3	Pre FT3	2(3)	2.31	3.27	0.500
		Post FT3	2(3)	0.00	0.00	
	L-T4 mcg	Pre L-T4 mcg	7(10)	128.57	44.32	0.197
		Post L-T4 mcg	7(10)	103.57	22.49	

TABLE 2: Comparison of clinical parameters before and after based on gender

TSH: thyroid-stimulating hormone, FT4: free T4, FT3, free T3, L-T4: levothyroxine

Table 3 compares thyroid hormones among age groups. The mean TSH level before and after BS showed statistically significant differences only in the 46-55 years age group (p = 0.012). Furthermore, we compared the mean FT4 and FT3 levels, as well as the mean L-T4 dose administered in the 36-45 years age group, and observed statistically significant differences in comparison to the other age groups (p < 0.05).

			Age (years)				
			<=25	26-35	36-45	46-55	>=56
TSH	Pre TSH	N(%)	5(7)	12(17)	21(30)	24(34)	4(6)
		Mean	2.31	3.18	4.00	6.39	1.58
		SD	1.02	2.25	2.43	6.29	1.69
	Post TSH	N(%)	5(7)	12(17)	21(30)	24(34)	4(6)
		Mean	2.53	3.36	2.80	3.93	0.84
		SD	1.85	2.78	2.16	3.38	0.99
	p value*		0.862	0.889	0.092	0.012	0.279
FT4	Pre FT4	N(%)	5(7)	12(17)	19(27)	23(33)	3(4)
		Mean	13.13	13.53	13.35	12.77	13.75
		SD	1.60	2.60	1.80	3.59	3.31
	Post FT4	N(%)	5(7)	12(17)	19(27)	23(33)	3(4)
		Mean	10.55	12.83	10.28	12.79	8.38
		SD	6.16	5.40	5.16	6.50	7.26
	p value*		0.450	0.639	0.013	0.987	0.420
FT3	Pre FT3	N(%)	3(4)	10(14)	9(13)	11(16)	2(3)
		Mean	3.96	3.39	3.03	2.10	0.00
		SD	1.04	1.89	1.79	2.05	0.00
	Post FT3	N(%)	3(4)	10(14)	9(13)	11(16)	2(3)
		Mean	2.87	3.11	1.55	1.28	0.00
		SD	2.55	2.36	1.84	1.81	0.00
	p value*		0.424	0.586	0.041	0.163	—
L-T4 mcg	Pre L-T4 mcg	N(%)	5(7)	7(10)	18(26)	23(33)	4(6)
		Mean	55.00	71.43	118.06	98.91	112.50
		SD	37.08	50.89	65.20	49.70	47.87
	Post L-T4 mcg	N(%)	5(7)	7(10)	18(26)	23(33)	4(6)
		Mean	50.00	60.71	87.50	84.78	81.25
		SD	30.62	57.48	42.23	38.24	23.94
	p value*		0.838	0.078	0.002	0.102	0.141

* p value<0.05 is considered statistically significant

TABLE 3: Comparison of clinical parameters before and after based on age

TSH: thyroid-stimulating hormone, FT4: free T4, FT3, free T3, L-T4: levothyroxine

Discussion

The available evidence supports the effectiveness of BS for treating obesity-related comorbidities [20-22]. Our study has demonstrated that BS can improve thyroid function, as indicated by the significant reductions seen in L-T4 doses and serum levels of TSH, FT4, and FT3. Several studies have demonstrated that BS-induced weight loss reduces TSH levels in euthyroid and hypothyroid patients [23,24]. In addition, BS affects the pharmacokinetics and bioavailability of drugs. Optimal T4 absorption requires an acidic stomach environment [25]. In 2020, Khan et al. [26] reported a significant reduction in thyroid replacement dose following BS among hypothyroidism patients. Although several comparative studies have been conducted, none have established the superiority of one surgical method over another in terms of improving thyroid function. It has been demonstrated that restrictive and bypass surgeries significantly reduce the thyrotropin-releasing hormone dose required [24,27-30]. LSG is a reliable first-line surgical option for super obesity and metabolic disorders. Furthermore, one-anastomosis gastric bypass (OAGB) has a similar surgical risk to LSG, but results in greater weight reduction [31].

Our findings suggest that BS alters TSH levels; however, further studies are needed to verify our results. Previous studies have provided contradictory findings regarding the association between TSH level and weight loss [32-36]. Although the present and previous studies have shown an association between thyroid hormone replacement and BS outcomes, the underlying mechanism is unclear. In adults with euthyroid obesity, a reduction in BMI indicates improved thyroid function. Moreover, surgical weight reduction has been associated with adipokine release, which affects thyroid hormone levels [23,37]. Leptin, a hormone secreted by adipose tissue, regulates the expression of the thyrotropin-releasing hormone gene [38]. A reduction in leptin level has been observed following weight loss induced by LSG or laparoscopic Roux-en-Y gastric bypass [39]. Weight loss following LSG is associated with a significant reduction in leptin levels, potentially leading to a decreased TSH level. LSG induces alterations in peptide hormone profiles, particularly those of pancreatic and intestinal origin, which are implicated in the metabolic benefits of BS [40,41]. In addition, BS induces alterations in serum FT3, FT4, and TSH levels by reducing adipose tissue. Studies have shown that obese individuals exhibit reduced expression of thyroid hormone receptor genes, particularly the TSH receptor, in both subcutaneous and visceral adipose tissue [42]. The primary mechanism through which adipokines, particularly leptin, affect thyroid hormone levels is widely accepted. Leptin, secreted by adipose tissue, stimulates thyroid function by elevating TSH and FT3 levels. Therefore, decreased leptin levels following surgery-induced weight loss and adipose tissue reduction can result in a low TSH level [43,44]. Treatment of morbid obesity can reduce elevations in the TSH level caused by the overactivation of the thyroid axis, in turn due to various pathophysiological processes and endocrine adaptations [45]. Studies have reported that ghrelin levels decrease following LSG and Roux-en-Y gastric bypass, whereas they remain unchanged after laparoscopic adjustable gastric banding [46]. Removal of the gastric fundus during surgery reduces ghrelin levels, which can affect TSH levels. Moreover, lowering ghrelin levels can also help reduce TSH levels, where weight loss triggers changes in hormone levels [47].

Our study had some limitations. First, thyroid function was evaluated by measuring L-T4 doses and serum TSH, FT4, and FT3 levels six months after surgery. Re-evaluating the same measures after 12 and 24 months, or longer, would have provided stronger evidence. TSH levels can be influenced by variables other than weight reduction following BS, despite the application of exclusion criteria, including drug use and thyroid disorders. For example, seasonal variations can lead to fluctuations in TSH levels, which decrease in summer and increase in winter [48]. Therefore, longitudinal studies with a larger sample are needed to confirm our findings. In addition, BMI was not recorded in all follow-up visits, which limited the valuation of the association between weight loss and thyroid profile improvement.

Our study had certain advantages as well. Unlike previous studies that only measured TSH levels, we evaluated L-T4 doses, as well as serum FT4 and FT3 levels. Our study emphasizes that morbidly obese individuals frequently exhibit a return to normal TSH levels following BS. Therefore, TSH values in these individuals should be interpreted with caution. Our results contribute to the growing knowledge of how obesity impacts thyroid hormones. Further research is needed to determine the factors driving low TSH levels after BS.

Conclusions

In conclusion, the results of our research indicate that bariatric surgery generally has a beneficial effect on patients suffering from hypothyroidism. Signs of this include an improved thyroid profile as well as a decreased amount of L-T4 dosage. The correlation between body mass index and thyroid hormones is further strengthened by this finding. This suggests that weight loss can have a positive impact on thyroid function and may reduce the need for medication in some cases.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Research Ethics Committee of Armed Forces Hospitals issued approval 2022-582. A formal ethical approval was obtained from both institutional review boards (IRB) of Directorate of Health Affairs -Taif HAP-02-T-067 - Approval Number (664), and IRB of Alhada Armed Forces Hospital, Taif - Approval number (2022-582). **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of**

interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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