

ASSESSING BASELINE THYROID-STIMULATING HORMONE (TSH) LEVELS IN PATIENTS WITH SEVERE OBESITY UNDERGOING PREOPERATIVE METABOLIC BARIATRIC SURGERY: A CROSS-SECTIONAL STUDY

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Abstract: Background: Severe obesity is a growing global health challenge, and metabolic bariatric surgery (MBS) is an effective treatment. However, the clinical relevance of routine preoperative thyroid assessments remains unclear. This cross-sectional study investigated the relationship between baseline thyroid-stimulating hormone (TSH) levels and other biochemical parameters during preoperative MBS.

Patients and Methods: Over 12 months (June 2024 to June 2025), 208 patients aged > 15 years undergoing preoperative evaluation for MBS at our referral center were considered for the study. Patients with prior bariatric/major abdominal surgery, active thyroid disease or thyroid-active medications (with a 3-month washout), or acute severe illness were excluded from the study. Fasting blood serum TSH was measured within one week before hospital admission, categorized using standard cutoffs, and statistical analysis was performed.

Results: The mean age and preoperative body mass index (BMI) were 36.6 ± 11.2 years and 43.7 ± 6.4 kg/m² (range 33.05-84.0), respectively. The serum TSH levels ranged from 0.02 to 14.13 (mean: 1.70 ± 1.46 mIU/L). The serum creatinine and albumin levels demonstrated a mean value of 61.3 ± 14.3 µmol/L (range: 37.8–155 µmol/L) and 43.2 ± 2.6 g/L (range: 36–50 g/L), respectively. Correlation analyses showed no statistically significant associations between TSH and age, BMI, HbA1c, hemoglobin, creatinine, or albumin levels (Pearson and Spearman coefficients). The prevalence of TSH abnormalities was not significantly different according to age group ($\chi^2 = 6.106$, $p = 0.978$) or gender ($\chi^2 = 1.445$, $p = 0.695$). Multivariable linear regression for log-transformed TSH showed that

age, BMI, HbA1c, and creatinine were not significant predictors. Most patients were euthyroid (92.8%), with 3.8% low TSH. Further, TSH levels showed no significant correlations with BMI ($r = 0.032$), hemoglobin, HbA1c, creatinine, or albumin, and did not differ by age group or gender.

Conclusions: These findings suggest that, in patients with severe obesity undergoing preoperative evaluation for MBS, TSH levels are generally within the reference range and are not statistically influenced by the measured biochemical or demographic factors. This supports a more clinically driven approach to thyroid testing while emphasizing the need for larger, multicenter, and longitudinal studies to clarify thyroid–obesity relationship and postoperative outcomes.

Keywords: severe obesity, metabolic bariatric surgery, thyroid, thyroid-stimulating hormone, obesity, TSH, body mass index.

INTRODUCTION

Obesity, particularly in its morbid form, has emerged as one of the most critical health challenges facing populations worldwide. The World Health Organization estimates that since 1975, the prevalence of obesity has tripled, with more than 650 million adults classified as obese globally (1). Severe obesity, often defined by a body mass index (BMI) of ≥ 40 kg/m² or greater than 35 kg/m² in the presence of significant obesity-related comorbidities, is associated with an increased risk of metabolic and cardiovascular disorders, certain cancers, and premature mortality. The range of metabolic bariatric surgery (MBS) procedures is rapidly expanding. Given the established efficacy of met-

abolic bariatric surgery (MBS) in achieving significant and sustainable weight loss, as well as improving or even reversing of obesity-related diseases (2–6), comprehensive preoperative assessment by a multidisciplinary healthcare team has become increasingly important with as these procedures become more widely available. This also comprises the optimal physiological status of the patient to be operated on. This assessment aims to optimize the physiological status of patients before surgery. Consequently, several issues arise during preoperative evaluation, including the role of thyroid function testing and the uncertain involvement of thyroid hormones in metabolism, body weight regulation, and overall metabolic health (7, 8). The TSH levels affect body weight in several ways. Thyroid hormones are major determinants of energy expenditure and lipid metabolism, and thus of general metabolic homeostasis. Studies have demonstrated an association between obesity and decreased TSH levels, especially elevated TSH levels, resulting from a state of central resistance to thyroid hormones (6). However, the prevalence and clinical relevance of TSH abnormalities at baseline among patients with severe obesity undergoing preoperative evaluation for MBS remain unclear.

Thyroid hormones (thyroxine (T4) and triiodothyronine (T3)) affect nearly every cell type in the body, increasing the metabolic rate, releasing lipids from cells and influencing glucose homeostasis (9). Even small variations in TSH or free thyroid hormone levels may affect body weight and body composition (10). Patients with hypothyroidism (elevated TSH levels and low thyroid hormone levels) typically experience weight gain despite decreased appetite, along with symptoms of slow metabolism including cold intolerance and bradycardia (11, 12). In contrast, patients with thyrotoxicosis commonly present with weight loss, hyperthermia, and increased metabolic rate.

Clinical and subclinical thyroid dysfunction are relatively common, and their prevalence appears to be increasing alongside the obesity epidemic (11). Recent epidemiological and clinical studies suggest a bidirectional relationship between thyroid homeostasis and adiposity. Elevated TSH values within the laboratory reference range have been associated with increased BMI, a greater amount of central fat and increased risk for metabolic syndrome in several studies (13). However, recent evidence suggests that preoperative TSH and free T4 levels are not significantly associated with weight loss following bariatric surgery in large patient cohorts (14).

Although several studies have reported increased rates of subclinical hypothyroidism among individuals with severe obesity, characterized by elevated TSH levels with normal T4 and T3 concentrations, these ab-

normalities are not necessarily accompanied by clinical signs or symptoms of hypothyroidism. Therefore, the clinical importance of routine TSH assessment in severely obese patients remains uncertain. Several studies have demonstrated that baseline thyroid function tests are normal in most patients, raising questions regarding the relevance of variations in TSH levels within the normal range (15).

Several studies have investigated the changes in thyroid hormone levels following MBS. For instance, Neves et al. observed a decrease in TSH levels in a group of obese women after weight loss. This preliminary study showed the TSH baseline profile and its associations with preoperative demographic, anthropometric, and biochemical parameters in a group of MBS candidates (16). Furthermore, overt hypothyroidism has been shown to improve following bariatric surgery, and patients often require lower doses of thyroid hormone replacement therapy (levothyroxine) after surgery (7).

The inconsistencies in the published literature, together with the clinical imperative for a thorough preoperative assessment, provided the motivation for the current investigation. Most previous studies suffer from limited sample sizes, incomplete assessment of associated health conditions, and inadequate adjustment for potential confounding factors. This study aimed to conduct a cross-sectional analysis of TSH levels in a cohort of 208 patients with severe obesity undergoing preoperative evaluation for MBS and assess its correlation with demographics and other biochemical parameters.

PATIENTS AND METHODS

Study Design and Ethical Considerations

This cross-sectional study was conducted at Dr. Sulaiman Al Habib Hospital-Olaya Branch, a tertiary referral center for MBS, over a 12-month period from June 2024 to June 2025. The study protocol was approved by the Institutional Review Board (IRB). All participants provided written informed consent prior to enrolment.

Patient selection criteria

The inclusion criteria were based on the standard indications for MBS, including a BMI below 35kg/m². The study population comprised all patients (aged ≥ 15 years) diagnosed with severe obesity who were scheduled to undergo MBS, specifically laparoscopic sleeve gastrectomy or Roux-en-Y gastric bypass, as their primary surgical intervention. Patients were provided with an informed consent form, either directly or through their guardians. Written informed consent from a parent/guardian was obtained from participants aged < 18 years, and ethical approval procedures were

followed with institutional regulations. Patients were excluded if they had undergone any prior bariatric surgical procedure or abdominal surgery, such as major upper gastrointestinal surgeries resulting in substantial anatomical or absorptive changes.

The exclusion criteria intended to omit patients with known current thyroid disease under active treatment (levothyroxine, antithyroid drugs) or use of medications known to markedly affect TSH levels within the prior 3 months (e.g., amiodarone, lithium, high-dose glucocorticoids), applying a three-month washout period to reduce acute medication-related distortion of TSH levels (17). However, due to the retrospective nature of data collection, medication information was incomplete and heterogeneous, limiting the ability to reliably confirm strict adherence to these medication-related exclusion criteria and the washout period. This limitation may have introduced residual confounding related to thyroid-active medication use.

Blood Sample Collection and Laboratory Analysis

Following approval for surgical intervention, each patient was informed of the study protocol and provided written informed consent. Subsequently, venous blood samples (5 mL) were collected from individual patients (fasting for more than 8 h) to measure serum TSH levels. Blood samples were collected early in the morning (8–10 a.m.) within one week before hospital admission for surgery. Samples were collected in serum separator (SST) tubes and transported to the central laboratory, where they were processed within 3–4 hours of collection. Serum was separated by centrifugation for 15 min and stored at 2–8 °C until analysis. Internal quality control (QC) procedures were performed every 24 hours, starting at 07:00, in accordance with the laboratory's standard operating procedures and manufacturer recommendations. Serum TSH was measured by a chemiluminescent microparticle immunoassay Assay (CMIA) using an Abbott ALINITY i machine. TSH status was then categorized based on the following standard cutoffs: low— < 0.3 ; normal— 0.3 to 4.5 ; mild elevation— 4.5 – 10 ; moderate elevation— 10 – 20 ; and severe elevation— > 20 mIU/L (18). All biochemical analyses were performed in the hospital's central laboratory using standardized spectrophotometric techniques with quality control measures to ensure accuracy and reproducibility.

Data collection and variables

were collected from each patient at the time of enrollment. Age was recorded in years, and gender was

documented as male or female. Anthropometric information, such as height and weight, was recorded to calculate BMI using the formula: weight in kilograms/height in meters squared (kg/m^2). The same fasting blood sample was used to determine TSH levels and biochemical parameters, including hemoglobin (g/dL), creatinine (mg/dL), albumin (g/dL), and glycated hemoglobin (HbA1c %). These variables were selected based on their relevance to the metabolic profile of patients with severe obesity and potential association with TSH levels.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean $\pm$ standard deviation (SD), and frequencies are reported as percentages. One-way analysis of variance (ANOVA) and chi-square tests were used to compare the means and percentages. Correlations among variables were assessed using both Pearson and Spearman correlation analyses. Spearman correlation was used to explore non-linear associations and reduce the influence of outlier values. A multivariable linear regression model was applied using log-transformed serum TSH levels as the dependent variable to address the right-skewed distribution of TSH. The independent variables included in the regression model were age, BMI, HbA1c, and creatinine. These variables were selected based on their clinical relevance to thyroid function and metabolic status.

The total number of patients included in the regression analysis was 208; however, HbA1c values were available for only 154 patients.

The coefficient of determination (R^2) indicates the proportion of variance in TSH levels explained by the model. All t -values were two-tailed, and a value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 208 patients with severe obesity who underwent MBS were included in the study, with a mean age of 36.6 ± 11.2 years (range, 15–66 years). The mean body weight was 116.6 ± 22.6 kg, and the mean height was 163.5 ± 9.3 cm. The preoperative BMI ranged from 33.05 to 84.0 kg/m^2 , with a mean of $43.7 \pm 6.4 \text{ kg/m}^2$, reflecting the severe obesity of the patients in the study cohort. The mean hemoglobin level was 13.8 ± 1.4 g/dL (range: 10.4–17.9 g/dL). TSH levels showed wide variability, ranging from 0.02 to 14.13 mIU/L, with a mean of 1.70 ± 1.46 mIU/L. Renal function assessed by serum creatinine levels

Table 1. Descriptive statistics of the study population

Parameters	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	Std. error
Age	208	15.00	66.00	36.59	11.17	0.29	0.17
Weight	208	71.00	196.00	116.60	22.59	0.77	0.17
Height	208	145.00	187.00	163.52	9.28	0.34	0.17
Before BMI	208	33.05	84.00	43.74	6.37	1.75	0.17
Hemoglobin	208	10.40	17.90	13.75	1.42	0.21	0.17
TSH	208	0.02	14.13	1.70	1.46	4.54	0.17
Creatinine	208	37.80	155.00	61.30	14.28	1.76	0.17
Albumin	176	36.00	50.00	43.16	2.64	-0.08	0.18

Table 2. Correlation of TSH with other parameters

Parameters	TSH				
	N	Pearson_r	Pearson_p	Spearman_r	Spearman_p
Age	208	0.027	0.697	0.078	0.262
Pre-operative BMI	208	0.032	0.647	0.094	0.175
Hemoglobin	208	-0.023	0.741	-0.031	0.653
HbA1C	154	0.072	0.374	0.091	0.261
Creatinine	208	-0.065	0.348	-0.023	0.74
Albumin	176	-0.037	0.625	-0.032	0.675

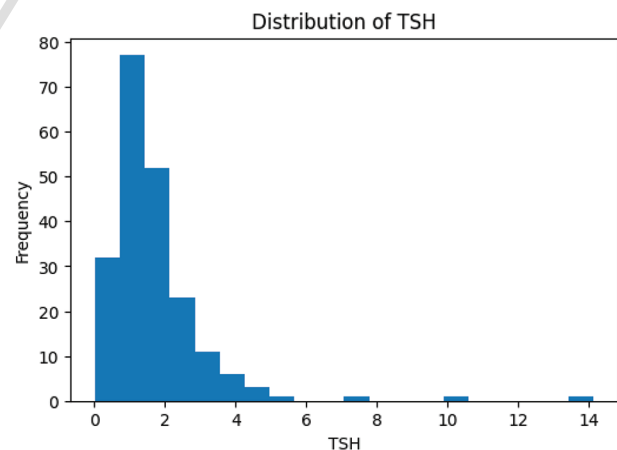
demonstrated a mean value of 61.3 ± 14.3 $\mu\text{mol/L}$ (range: 37.8–155 $\mu\text{mol/L}$). Serum albumin, available for 176 patients, ranged between 36 and 50 g/L, with a mean value of 43.2 ± 2.6 g/L (Table 1).

Distribution of Serum TSH Levels

The histogram of serum TSH values (Figure 1) demonstrates a markedly right-skewed distribution, with the majority of participants having TSH concentrations clustered between approximately 0.5–3.0 mIU/L. Only a small number of participants exhibited elevated TSH levels beyond 5 mIU/L, with a few extreme outliers reaching values above 10 mIU/L.

Correlation analysis between TSH and clinical variables

To explore possible associations between thyroid-stimulating hormone (TSH) levels and other clinical and biochemical parameters, we performed both Pearson and Spearman correlation analyses. As shown in Table 2, the Pearson correlation coefficients between TSH and all examined parameters were uniformly weak and did not reach statistical significance. The highest positive correlation was observed with HbA1c ($r = 0.072$, $p = 0.374$), followed by pre-operative BMI ($r = 0.032$, $p = 0.647$) and age ($r = 0.027$, $p = 0.697$). It was negatively correlated with creatinine ($r = -0.065$,

**Figure 1.** Histogram showing the distribution of serum TSH values

$p = 0.348$), albumin ($r = -0.037$, $p = 0.625$) and hemoglobin ($r = -0.023$, $p = 0.741$). None of these associations attained conventional levels of statistical significance, suggesting null or weak linear association between TSH and these metabolic markers in this cohort.

Since TSH values were right-skewed in the descriptive analysis, Spearman rank correlation coefficients were employed to explore possible nonlinear associations and to reduce the influence of outliers. The Spearman correlations produced results that were similar to the Pearson analysis, with all coefficients being weak and non-significant. The strongest Spearman

correlation was with pre-operative BMI ($\rho = 0.094$, $p = 0.175$), followed by HbA1c ($\rho = 0.091$, $p = 0.261$) and age ($\rho = 0.078$, $p = 0.262$). Non-significant negative correlation was found for creatinine ($\rho = -0.023$, $p = 0.740$), hemoglobin ($\rho = -0.031$, $p = 0.653$) and albumin ($\rho = -0.032$, $p = 0.675$). The fact that the Pearson and Spearman results agree suggests that the lack of association is not an artifact of the skewed TSH distribution, but rather a true lack of linear relationships between TSH and the tested variables.

The correlation heatmap displays the relationships between the variables studied in this work (Figure 2). Most correlations between the variables were weak and fell within the central part of the color scale. TSH showed minimal correlation with age, BMI, HbA1c, creatinine, and albumin. However, there were stronger correlations between the biochemical parameters that were not associated with TSH, such as albumin and creatinine, which may reflect their involvement in nutritional and metabolic processes. The heatmap data support the present findings that serum TSH levels did not correlate with the majority of the analyzed variables.

TSH distribution across age and gender groups

As shown in Table 3, 193 of 208 patients (92.8%) had normal TSH levels within the reference range of 0.3–4.5 mIU/L. Among the other 15 patients (7.2%) abnormal values of TSH were found to be the least common abnormality. Low TSH (< 0.3 mIU/L) was seen in 8 patients (3.8%). Mildly elevated TSH

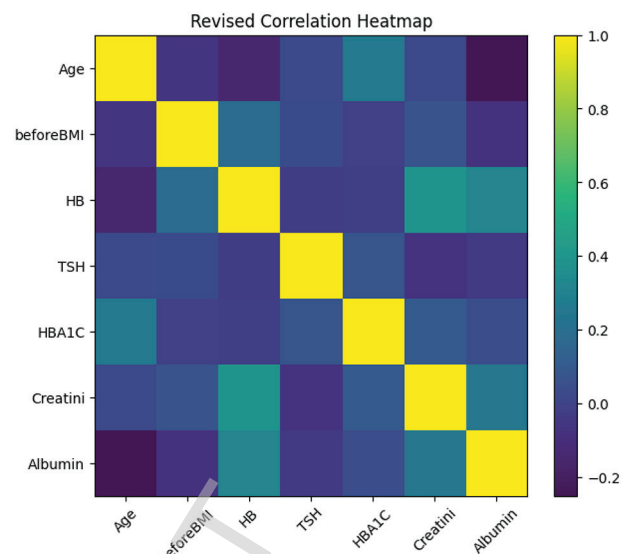


Figure 2. Correlation heatmap among clinical and biochemical variables

(The heatmap is a square grid matrix where the strength and direction of the correlations are represented by the intensity of the color from dark purple (negative correlations) to bright yellow (positive correlations)).

(4.5–10 mIU/L) was seen in 5 (2.4%) patients and moderately elevated TSH (10–20 mIU/L) was seen in 2 (1.0%) patients. Crucially, no patient in this cohort had TSH levels > 20 mIU/L, indicating that there was no overt hypothyroidism in the study population.

The rate of TSH abnormalities differed between age groups, although the overall numbers were low. The most common age group for low TSH was 41–50

Table 3. Prevalence of TSH level abnormality among age and gender group

Categories	TSH (n, %)						Pearson chi-square (χ^2 , df, p)
	Low	Normal	Mild elevated	Moderately elevated	Severe elevation	Total	
Age group							
1 (15-20 yrs)	0 (0.0)	14 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	14 (100.0)	$\chi^2 = 6.106$; df = 15; p = 0.978
2 (21-30 yrs)	1 (2.0)	48 (94.1)	1 (2.0)	1 (2.0)	0 (0.0)	51 (100.0)	
3 (31-40 yrs)	3 (4.3)	65 (92.9)	2 (2.9)	0 (0.0)	0 (0.0)	70 (100.0)	
4 (41-50 yrs)	3 (5.8)	47 (90.4)	1 (1.9)	1 (1.9)	0 (0.0)	52 (100.0)	
5 (51-60 yrs)	1 (6.7)	13 (86.7)	1 (6.7)	0 (0.0)	0 (0.0)	15 (100.0)	
6 (61-70 yrs)	0 (0.0)	6 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (100.0)	
Total (n = 208)	8 (3.8)	193 (92.8)	5 (2.4)	2 (1.0)	0 (0.0)	208 (100.0)	
Gender group							
Male	2 (2.5)	75 (94.9)	1 (1.3)	1 (1.3)	0 (0.0)	79 (100.0)	$\chi^2 = 1.445$; df = 3; p = 0.695
Female	6 (4.7)	118 (91.5)	4 (3.1)	1 (0.8)	0 (0.0)	129 (100.0)	
Total (n = 208)	8 (3.8)	193 (92.8)	5 (2.4)	2 (1.0)	0 (0.0)	208 (100.0)	

TSH level categories were as follows: low: < 0.3 ; normal: 0.3–4.5; mildly elevated: 4.5–10; moderately elevated: 10–20; and severely elevated: > 20 mIU/L.

years with 3 of 52 patients (5.8%) having TSH below 0.3 mIU/L. The 51–60 years group also had a relatively high proportion of low TSH, with 1 of 15 patients (6.7%) affected. Mildly elevated TSH was common in the 51–60 years group with 1 out of 15 patients (6.7%) in this group, followed by the 31–40 years group with 2 out of 70 patients (2.9%) having mildly elevated levels. Moderately elevated TSH was present only in the 21–30 years and 41–50 years groups (one patient, 2.0%, and one patient, 1.9%, respectively). No TSH abnormalities were found in the two youngest (15–20 years) and oldest (61–70 years) age groups. All patients in these groups had normal TSH levels. Although these obvious differences, there was no statistically significant association between age group and TSH category as assessed by Pearson chi-square test ($\chi^2 = 6.106$, $df = 15$, $p = 0.978$) indicating the prevalence of TSH abnormalities was similar in all ages.

Some differences were observed in the frequency of TSH abnormalities when results were analyzed by gender, but these were not statistically significant either. Among male patients, 2 of 79 (2.5%) had low TSH, 1 of 79 (1.3%) had mildly elevated TSH, 1 of 79 (1.3%) had moderately elevated TSH, and 75 of 79 (94.9%) had normal levels. Of the 129 female patients, 6 (4.7%) had low TSH, 4 (3.1%) had mildly elevated TSH and 1 (0.8%) had moderately elevated TSH, while 118 (91.5%) had normal TSH levels. The prevalence of low TSH was almost two-fold higher in females than in males (4.7% vs. 2.5%) and mildly elevated TSH was also more common in females (3.1% vs. 1.3%). However, the chi-square test did not demonstrate a significant difference between genders ($\chi^2 = 1.445$, $df = 3$, $p = 0.695$). In the results of this study, the prevalence of abnormal TSH levels showed no significant difference between the sexes.

The prevalence of TSH abnormalities in this cohort was low in general, with > 92% of patients having a normal TSH. Clinically significant thyroid dysfunction defined by extreme TSH deviations is uncommon in this preoperative bariatric surgery population. None of the patients had severely elevated TSH (> 20 mIU/L) and very few patients were in abnormal categories (15 patients total). There was no significant

correlation between age and sex, indicating that demographic variables are not strong predictors of TSH status in this cohort. The implications of these findings are relevant to preoperative screening, as they suggest that routine testing for TSH will detect abnormalities in a very small percentage of patients and targeted screening based on age or gender may be no better than universal screening. However, a small minority of patients with low or raised TSH require clinical attention, as they may need further endocrine assessment and possible optimisation of thyroid function prior to surgery to reduce perioperative risks.

Multivariable linear regression analysis for TSH

The difference was not statistically significant ($\chi^2 = 1.445$, $df = 3$, $p = 0.695$) (Table 4). To test the independent effects of age, BMI, HbA1c, and creatinine on serum TSH levels, multivariable linear regression analysis was performed on log-transformed TSH values. The overall model was not significant ($F = 1.039$, $p = 0.389$). Altogether, the independent variables tested explained only 2.7% of the variance in the log-transformed serum TSH values ($R^2 = 0.027$; adjusted $R^2 = 0.001$). The individual effects of the independent variables tested against log-transformed TSH values are listed in Table 4. The age of the patient tested against the log-transformed TSH values showed a non-significant positive effect ($p = 0.106$; $\beta = 0.0083$). The patient's HbA1c tested against the log-transformed TSH values also showed a non-significant positive effect ($p = 0.458$; $\beta = 0.0481$). The patients' BMI and creatinine levels tested against the log-transformed TSH values each resulted in non-significant effects ($p = 0.924$; $\beta = 0.0009$ and $p = 0.996$; $\beta = -2.225 \times 10^{-5}$, respectively). None of the tested clinical variables had an independent effect on TSH levels after accounting for the possible confounding effects of the other tested variables. All independent variables were tested for association with TSH after log transformation of the latter variable to control for potential confounders. The result for age was a positive but non-significant trend of very small magnitude ($\beta = 0.0083$, $p = 0.106$; adjusted $R^2 = 0.001$). HbA1c showed a positive trend of very small

Table 4. Multivariable linear regression analysis for log-transformed TSH

Variable	β	Standard Error	t	p-value
(Constant)	-0.201	0.340	-0.592	0.555
Age	0.0083	0.005	1.622	0.106
BMI	0.0009	0.009	0.095	0.924
HbA1c	0.0481	0.065	0.743	0.458
Creatinine	-2.225×10^{-5}	0.004	-0.005	0.996

magnitude that was also not significant ($\beta = 0.0481$, $p = 0.458$). BMI and creatinine levels showed no association with log-transformed TSH ($\beta = 0.0009$, $p = 0.924$; and $\beta = -2.225 \times 10^{-5}$, $p = 0.996$, respectively). The model showed a Durbin-Watson statistic of 2.033 (not significant), indicating that there was no evidence of serial correlation in the residuals. On the other hand, the Omnibus and Jarque-Bera tests, both measuring the overall normality of the residuals, were statistically significant, indicating skewness and/or other types of departure from normality in the residuals. Despite the log transformation of TSH, some deviation from the normal distribution persisted. Overall, the regression findings support the conclusion that serum TSH levels were not independently associated with age, BMI, or other tested parameters in the studied population.

DISCUSSION

This cross-sectional study evaluated TSH levels, in a large cohort of 208 patients with severe obesity who underwent preoperative evaluation for MBS at our institution. The principal findings indicate that the vast majority of this cohort exhibited TSH levels within the normal reference range, with no statistically significant correlation observed between TSH and clinical variables, including BMI, hemoglobin, HbA1c, renal function (creatinine), serum albumin, age, or gender. These findings offer significant insights into the thyroid status of individuals with severe obesity who are preparing for MBS and contribute to the ongoing discourse on the clinical significance of thyroid assessment in this demographic. In the present study, no association was observed between TSH levels and obesity-related parameters. However, previous studies have reported elevated TSH levels among individuals with obesity (6). The TSH levels in the present study are described together with the baseline characteristics of the study cohort, which were used to analyze the TSH distribution and its association with several clinical parameters. The predominance of normal TSH values observed in our cohort is consistent with recent studies demonstrating euthyroid status in most patients with severe obesity, despite the recognized potential for subtle alterations in thyroid axis regulation associated with obesity (3).

The lack of correlation between TSH and BMI in this cohort counters earlier reports suggesting a positive association between elevated TSH and increased adiposity and supports an emerging paradigm in which obesity-related shifts in thyroid hormone levels represent physiological responses rather than pathological thyroid dysfunctions (19,20). The lack of any association may be due to the fact that the TSH values in

the vast majority of patients were in the normal range; therefore, the study lacked the statistical power to assess any relationship. The relationship between obesity and TSH levels may be non-linear or mediated by other untested variables, including leptin, insulin resistance, or markers of inflammation (13). The weak non-significant correlations between TSH and HbA1c support the view that TSH levels in euthyroid individuals with obesity is not associated with glycemic control or metabolic syndrome (21). This contrasts with other reports in which a positive association between TSH and various markers of insulin resistance has been reported (22). The basis for these differences between studies includes the composition of the study populations, the TSH values measured, and whether patients with known thyroid disease were included. Our correlation studies support the view that preoperative MBS candidates' serum TSH values are not correlated with a variety of commonly assessed clinical, anthropometric, and biochemical parameters.

Moreover, the weak correlation with hemoglobin and albumin indicates that thyroid status has little influence on the regulation of erythropoiesis or protein metabolism in this preoperative setting. The limited range of TSH values observed in the majority of patients (92.8% remained within the normal reference interval) may have contributed to limited statistical power to detect associations. Alternatively, the relationship between TSH and metabolic parameters may be more complex and non-linear, or may be confounded by other factors not measured in this study such as leptin levels, inflammatory markers or the presence of subclinical thyroid disease. Nevertheless, these results give a clear and robust description of the lack of association between TSH and major clinical variables in this particular cohort, thus guiding the subsequent analysis of TSH abnormality prevalence and its demographic distribution.

Notably, substantial evidence suggests that mild TSH elevations observed in some individuals with obesity may be secondary to leptin-mediated hypothalamic-pituitary activation and alterations in peripheral thyroid hormone metabolism, mechanisms that are hypothesized to optimize energy expenditure under conditions of excess adiposity (5, 6, 23). Furthermore, the lack of significant variation by age and gender suggests that severe obesity may overshadow the usual demographic patterns in abnormal TSH prevalence, despite trends toward a slight female predominance (5, 7). There was no statistically significant difference in the prevalence of TSH abnormalities between males and females. This may be due to random variations. Although thyroid disorders, especially in hypothyroidism, are more prevalent in the general population, par-

ticularly females (24), in this specific cohort of severely obese patients scheduled for MBS, the gender disparity was not pronounced enough to be statistically significant. The lack of any significant association between TSH status and age is also noteworthy. It is well established that TSH levels changes with increasing age (25). In the general population, for example, TSH levels tend to increase with age, and the upper limit of the normal range for TSH increases for older individuals. Conventional preoperative TSH levels testing may merely indicate physiological adaptations rather than clinically significant thyroid disorders, as the majority of severe obese bariatric candidates have euthyroid profiles. Longitudinal MBS studies challenge the need for comprehensive preoperative thyroid screening in the absence of a clinical rationale, revealing that substantial surgical weight loss normalizes modest TSH level irregularities (5, 7, 26).

Limitation and Strengths

This cross-sectional study has several limitations. First, it was conducted at a single center which may limit the generalizability of the findings to other populations with different demographic and clinical characteristics. Second, medication data were incomplete and heterogeneous due to the retrospective dataset, which affected the reliability of confirming exclusion of patients on thyroid-active medications and adherence to the intended three-month washout period. This incomplete medication information may have introduced residual confounding related to thyroid-active medication use, potentially impacting the interpretation of TSH levels in the cohort. Third, the lack of measurement of free T4 and free T3 in euthyroid patients precludes a complete assessment of thyroid hormone homeostasis and peripheral thyroid hormone activity. Fourth, the HbA1c data was not uniformly available for all the patients and hence was not precluded its inclusion in the regression model as a covariate, potentially affecting the completeness of multivariable analysis.

Despite these limitations, this study has several strengths. The number of patients included in this cross-sectional study was adequate, enhancing the reliability of the findings. Blood samples were collected prospectively, after a standardized fast of at least 8 hours, reducing variability. Patients were studied at the same time of day to minimize the effects of natural diurnal variations in thyroid hormone levels. Patients taking thyroid-active medications at the time of the study were specifically excluded, strengthening the validity of TSH measurements in the cohort. Furthermore, this study provides a detailed characterization of

TSH distribution and its associations with clinical and biochemical variables in a well-defined population of patients with severe obesity undergoing preoperative evaluation for metabolic bariatric surgery.

Clinical implications

This study has several implications for the clinical management of patients before and after MBS. The findings suggest the targeted screening of patients prior to MBS for overt thyroid dysfunction, particularly hypothyroidism, as these conditions can have a significant impact on patients' postoperative recovery and may pose additional surgical risks. The findings of this study also suggest that random testing for slight elevations in TSH in overweight/obese individuals may not be indicated, as the increase in TSH is likely to reflect an adaptive response to excess body fat. Importantly, the assessment of only TSH in the post-MBS period is of limited value, as it does not accurately reflect the patient's thyroid status, and a more comprehensive assessment may be required in select cases to optimize their management. Furthermore, the cross-sectional design and single-center setting of this study indicate that longitudinal monitoring and broader population studies are needed to better understand the long-term impact of MBS on thyroid physiology and to refine screening protocols accordingly.

CONCLUSION

In conclusion, no significant association was observed between TSH levels and BMI or other biochemical markers among the 208 study participants during their preoperative MBS. Serum TSH values showed a non-normal distribution based on the Shapiro–Wilk test. Therefore, non-parametric Spearman correlation analyses and log-transformed regression models were used. Correlation analysis demonstrated no significant association between TSH levels and major clinical or biochemical parameters. Multivariable regression analysis adjusted for age, BMI, HbA1c, and creatinine showed that none of these variables were independently associated with the log-transformed TSH values. TSH levels ranged from 0.02 to 14.13 mIU/L (mean 1.70 ± 1.46), with most patients being euthyroid (92.8%); 3.8% had low TSH, 2.4% had mild elevation, 1.0% had moderate elevation, and no patients had severe elevations. Interpreting these null associations, the authors argue that minor TSH variations in patients with severe obesity may reflect adaptive physiology rather than clinically meaningful thyroid disease and raise the possibility that indiscriminate thyroid testing may yield a low diagnostic return in similar populations. However, studies linking thyroid status to

perioperative outcomes, management changes, and cost-effectiveness are required before screening strategies can be recommended for this purpose. Considering the limitations of this study, further longitudinal studies are warranted to optimize TSH levels in patients who have undergone bariatric surgery.

Abbreviations

MBS - Metabolic bariatric surgery

TSH - Thyroid stimulating hormone

BMI - Body mass index

IRB - Institutional review board

CMIA - Chemiluminescent Microparticle Immunoassay Assay

QC - Quality control

ANOVA - One-way analysis of variance

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Note: Artificial intelligence was not utilized as a tool in this study.

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Sažetak

PROCENA BAZALNIH NIVOVA TIREOSTIMULIRAJUĆEG HORMONA (TSH) KOD PACIJENATA SA TEŠKOM GOJAZNOŠĆU PRE METABOLIČKE BARIJATRIJSKE HIRURGIJE: STUDIJA PRESEKA

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Uvod: Teška gojaznost predstavlja rastući globalni zdravstveni problem, dok metabolička barijatrijska hirurgija (MBS) predstavlja efikasan način lečenja. Međutim, klinički značaj rutinske preoperativne procene funkcije štitaste žlezde još uvek nije jasno definisan. Ova studija preseka ispitala je povezanost bazalnih vrednosti tireostimulirajućeg hormona (TSH) sa drugim biohemijskim parametrima kod pacijenata tokom preoperativne procene za metaboličku barijatrijsku hirurgiju.

Ispitanici i metode: Tokom perioda od 12 meseci (od juna 2024. do juna 2025. godine), u studiju je uključeno 208 pacijenata starijih od 15 godina koji su bili podvrgnuti preoperativnoj proceni za metaboličku barijatrijsku hirurgiju (MBS) u našem referentnom centru. Iz studije su isključeni pacijenti sa prethodnim barijatrijskim zahvatima ili velikim abdominalnim operacijama, aktivnim oboljenjem štitaste žlezde, primenom lekova koji utiču na funkciju štitaste žlezde (uz period obustave terapije od 3 meseca), kao i pacijenti sa akutnim teškim oboljenjima. Nivo TSH u serumu određen je iz uzorka krvi nakon gladovanja, u periodu od nedelju dana pre prijema u bolnicu, vrednosti su klasifikovane prema standardnim referentnim granicama, a zatim je izvršena statistička analiza.

Rezultati: Prosečna starost ispitanika iznosila je $36,6 \pm 11,2$ godina, dok je prosečan preoperativni indeks telesne mase (BMI) iznosio $43,7 \pm 6,4$ kg/m² (raspon: 33,05–84,0 kg/m²). Vrednosti TSH u serumu kretale su se od 0,02 do 14,13 mIU/L, sa prosečnom vrednošću od $1,70 \pm 1,46$ mIU/L. Prosečne vrednosti kreatinina i albumina u serumu iznosile su $61,3 \pm 14,3$ μmol/L (raspon: 37,8–155 μmol/L) i $43,2 \pm 2,6$ g/L (raspon: 36–50 g/L).

Analiza korelacije nije pokazala statistički značajnu povezanost između nivoa TSH i starosti, BMI, HbA1c, hemoglobina, kreatinina ili albumina (prema Pearsonovom i Spearmanovom koeficijentu korelacije). Učestalost odstupanja vrednosti TSH nije se statistički značajno razlikovala u odnosu na starosne grupe ($\chi^2 = 6,106$; $p = 0,978$) niti u odnosu na pol ($\chi^2 = 1,445$; $p = 0,695$). Multivarijantna linearna regresiona analiza logaritamski transformisanih vrednosti TSH pokazala je da starost, BMI, HbA1c i kreatinin nisu bili značajni prediktori nivoa TSH. Većina pacijenata bila je eutireoidna (92,8%), dok je kod 3,8% pacijenata zabeležen snižen nivo TSH. Dodatno, nivoi TSH nisu pokazali statistički značajnu povezanost sa BMI ($r = 0,032$), hemoglobinom, HbA1c, kreatininom ili

albuminom, niti su se razlikovali u odnosu na starosnu grupu ili pol.

Zaključak: Ovi nalazi ukazuju na to da su kod pacijenata sa teškom gojaznošću koji se podvrgavaju preoperativnoj proceni za metaboličku barijatrijsku hirurgiju (MBS) vrednosti TSH uglavnom u granicama referentnog opsega i da nisu statistički povezane sa ispitivanim biohemijskim ili demografskim faktorima. Rezultati po-

državaju individualizovan, klinički usmeren pristup proceni funkcije štitaste žlezde, uz naglašavanje potrebe za većim multicentričnim i longitudinalnim studijama radi boljeg razumevanja povezanosti funkcije štitaste žlezde i gojaznosti, kao i uticaja na postoperativne ishode.

Cljučne reči: teška gojaznost, metabolička barijatrijska hirurgija, štitasta žlezda, tireostimulirajući hormon, gojaznost, TSH, indeks telesne mase.

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