Predictors of Hypothyroidism after Thyroid Lobectomy

Shafi Shadhar Thahab[1] Ammar M. S. Almomin[1] Qusay B.J. Al-Zajaji[2] Abbas A. Mansour[1]

[1] Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), University of Basrah, Basrah, Iraq
[2] Al-Hassan Metabolism, Endocrine and Diabetes Center (HMEDC), Karbala Health Directorate, Karbala, Iraq

Address for correspondence Ammar M. S. Almomin, MD, Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), University of Basrah, Basrah 60100, Iraq (e-mail: Ammar.Mohammed@uobasrah.edu.iq).

Ibnosina J Med Biomed Sci 2023;15:129–134.

Abstract

Background The reported incidence of postlobectomy hypothyroidism is quite different among studies with an average of 22%. Many risk factors predict the development of hypothyroidism in patient undergoing thyroid lobectomy.

Aim The aim of this study was to assess predictors of hypothyroidism after thyroid lobectomy.

Methods A retrospective observational study was conducted at Faiha Specialized Diabetes, Endocrine, and Metabolism Center and Zain Alabdeen Teaching Hospital during a period of 9 months from January 2022 to October 2022. It included data of 80 patients collected from medical archives for individuals who had thyroid lobectomy regardless the cause. Information was collected regarding patient pre- and postlobectomy thyroid-stimulating hormone (TSH), thyroid peroxidase antibody, and antithyroglobulin antibody levels.

Results In this study, 22.5% of patients developed hypothyroidism after lobectomy. Preoperative TSH level was substantially higher than average in patients who developed postlobectomy hypothyroidism than those who did not. The highest prevalence of postlobectomy hypothyroidism was seen significantly in patients with positive thyroid peroxidase autoimmunity and in those with positive thyroglobulin autoimmunity. Preoperative TSH level more than 2.61 mIU/L is a predictor for the risk of postlobectomy hypothyroidism.

Conclusion Higher TSH level and thyroid autoimmunity predict higher risk of developing hypothyroidism after thyroid lobectomy.

Keywords
- hypothyroidism
- Iraq
- lobectomy
- predictors
- thyroid

Introduction

Thyroid disorders can affect one or both lobes. Unilateral removal (lobectomy) can be optimal for toxic adenoma, cytologically indeterminate nodules, and low risk differentiated thyroid cancer (DTC).[1] Many factors affect thyroid function such as age, gender, race, time of day, season, dietary iodine level, socioeconomic status, stress, body mass index (BMI), immune status, phase of menstrual cycle, and overall individual wellbeing.[2] The prevalence of

article published online
July 20, 2023

DOI https://doi.org/10.1055/s-0043-1770927.
ISSN 1947-489X.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

postoperative hypothyroidism depends on the duration of follow-up after surgery and on the criteria used to define hypothyroidism.[3]

The reported incidence of postlobectomy hypothyroidism is quite different among studies, with an average of 22%.[4] Varying levels of its definitions also complicate the diagnosis of hypothyroidism. The National Health and Nutrition Examination Survey III suggested 0.4 to 4.0 mIU/L as the thyroid-stimulating hormone (TSH) reference range. However, others have suggested upper limits of 3.59, 5.5, 7.0, 8.0, and 10.0 mIU/L. This makes interinstitutional and pooled data sets difficult to be interpreted or generalized.[5]

Many risk factors predict the development of hypothyroidism in patients undergoing thyroid lobectomy. Patient age at the time of surgery is strongly correlated with the final thyroid outcome. It is a relevant clinical predictor of future hypothyroidism and the need for thyroid hormone replacement.[6] Higher preoperative TSH level translates into higher posthemithyroidectomy hypothyroidism. However, a definite cutoff point has yet to be established.[5] The presence of thyroid peroxidase antibody (TPO) was the most well-studied risk factor. The literature reviewed that hypothyroidism posthemithyroidectomy ranges from 38.9 to 59%.[7] Lymphocytic infiltration of the gland carries a higher incidence of hypothyroidism. Furthermore, the magnitude of the lymphocytic infiltration also has some influence, with 49% for high-grade infiltration and 10% for low-grade in cases undergoing surgery.[8] Derived weight ratio is the proportion of thyroid lobe remnant (as calculated from ultrasonographic dimensions) to the total body weight, which is considered a predictor of postoperative thyroid failure. A higher incidence of postoperative hypothyroidism is associated with a derived ratio of less than 0.08 g/kg.[9] Antithyroglobulin antibody (ATA) and thyroid peroxidase antibody preoperatively might predict subclinical thyroiditis, which is the ultimate result of an inflammatory process by thyroid antigens and its antibodies.[10,11] Serial postoperative assessments for any sign or symptom of hypothyroidism are advisable.[12] Starting 1 month postoperatively, followed by subsequent evaluations depending on the initial laboratory results.[1]

Unlike previous clinical practice, recent medical approaches are directed against the routine use of levothyroxine after hemithyroidectomy. This will obviate the adverse effects of replacement therapy, particularly in postmenopausal women.[10] However, levothyroxine prescription or discontinuation depends mainly on TSH levels postoperatively.[13] The mean time from surgery to detection of hypothyroidism varies between studies and ranges from 4 to 8 months. About 90% of patients who develop hypothyroidism are detected within the first-year postsurgery.[14]

This study aimed to assess the predictors of hypothyroidism after thyroid lobectomy.

Patients and Methods

Setting and Design

This was a retrospective observational study that was conducted at Faiha Specialized Diabetes, endocrine, and Metabolism Center (FDEMC) and Zain Alabdeen Teaching Hospital during a period of 9 months from January 2022 to October 2022. The study included documented data from medical archives of 80 patients who had thyroid lobectomy regardless of the cause, ethnicity, age, gender, and comorbid conditions. Only preoperative euthyroid patients were included (defined as TSH level between 0.5 and 5.5 mIU/L). We excluded patients with preoperative hypothyroidism (defined as TSH level > 5.5 mIU/L) or taking levothyroxine and patients with a history of radiation, and those undergone previous thyroid surgery.

Data Collection

Information was collected regarding the patient's age, sex, occupation, residence, history of hypertension, BMI, pathology, and surgical procedure, pre- and postlobectomy TSH, TPO, and ATA levels.

Statistical Analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. The data are presented as mean, standard deviation, and ranges. Frequencies and percentages present categorical data. An independent *t*-test (two-tailed) was used to compare TSH levels according to postlobectomy thyroid status. The chi-squared test assessed the association between postlobectomy thyroid status and certain risk factors. Receiver operating characteristic (ROC) curve analysis was constructed for preoperative TSH level to predict postlobectomy hypothyroidism. The sensitivity, specificity, and accuracy of serological markers were calculated. A level of *p*-value less than 0.05 was considered significant.

Results

The total number of patients was 80. Their age ranged from 32 to 81 years, with a mean of 46.42 ± 11.3 years. Females were predominant (72.5%) in the studied population. In this study, only 23.8% of patients had normal BMI; the vast majority were obese or overweight. Benign pathology was diagnosed in 67.5% of patients, and the most common surgical approach used for lobectomy was the classical procedure (65%). We noticed that 22.5% of study patients developed hypothyroidism after lobectomy, as shown in ►**Table 1**. In this study, preoperative TSH level was substantially higher in patients who developed postlobectomy hypothyroidism than those who did not (3.12 vs. 1.99 mIU/L). The highest prevalence of postlobectomy hypothyroidism was seen significantly in patients with positive thyroid peroxidase autoimmunity 44.1% and those with positive thyroglobulin autoimmunity 38.9%. No statistically significant associations were detected ($p \geq 0.05$) between the incidence of postlobectomy hypothyroidism and patient risk factors profile except for preoperative TSH level and autoimmune thyroid antibodies markers, as shown in ►**Table 2**.

ROC curve analysis was constructed for preoperative TSH level to predict postlobectomy hypothyroidism. As shown in ►**Fig. 1**, the cutoff point of preoperative TSH level was 2.61 mIU/L. So, preoperative TSH level more than 2.61 mIU/L

Table 1 General characteristics of patients undergoing thyroid lobectomy

Variable		*n* (%)
Gender	Females	58 (72.5)
	Males	22 (27.5)
Body mass index (BMI)	Normal	19 (23.8)
	Overweight	44 (55.0)
	Obese	17 (21.2)
Hypertension		37 (46.3)
Malignant pathology		26 (32.5)
Thyroid peroxidase autoimmunity		34 (42.5)
Thyroglobulin autoimmunity		36 (45.0)
Previous surgical approach for lobectomy	Classical	52 (65.0)
	Minimally invasive	19 (23.8)
	Endoscopic	9 (11.2)

predicts the risk of postlobectomy hypothyroidism (area under the curve = 74%). Preoperative TSH level was 60% sensitive, 89.7% specific, and 75.6% accurate for predicting future hypothyroidism (as shown in ►**Table 3**).

Autoimmune thyroid antibodies provide additional predictive value for the development of future hypothyroidism.

Discussion

For some thyroid problems, thyroid lobectomy has historically been considered a safe and successful surgical treatment. Although the contralateral lobe remains intact, there is a possibility of developing hypothyroidism after surgery. The reported incidence ranges between 9 and 49%.[15] Compared to total thyroidectomy, lobectomy has a significantly lower rate of complications, and most patients do not require thyroid hormone replacement.[14] This study reported a 22.5% chance of postlobectomy hypothyroidism, which agrees with the Cho et al's study, in which, following thyroid

Table 2 Association between patient characteristics and postlobectomy hypothyroidism

General characteristics	Postlobectomy		Total (%) $n = 80$	*p*-Value
	Hypothyroid[a] (%) $n = 18$	Euthyroid[b] (%) $n = 62$		
Age (year)				
< 40	3 (17.6)	14 (82.4)	17 (21.3)	0.704
40–59	9 (21.4)	33 (78.6)	42 (52.5)	
≥ 60	6 (28.6)	15 (71.4)	21 (26.3)	
Sex				
Male	6 (27.3)	16 (72.7)	22 (27.5)	0.528
Female	12 (20.7)	46 (79.3)	58 (72.5)	
BMI level				
Normal	2 (10.5)	17 (89.5)	19 (23.8)	0.206
Overweight	10 (22.7)	34 (77.3)	44 (55.0)	
Obese	6 (35.3)	11 (64.7)	17 (21.3)	
Pathology				
Benign	10 (18.5)	44 (81.5)	54 (67.5)	0.219
Malignant	8 (30.8)	18 (69.2)	26 (32.5)	
Surgical approach				
Classical	11 (21.2)	41 (78.8)	52 (65)	0.898
Minimal invasive	5 (26.3)	14 (73.7)	19 (23.8)	
Endoscopic	2 (22.2)	7 (77.8)	9 (11.3)	
Preoperative TSH	3.12 ± 1.2	1.99 ± 0.87		0.001
Thyroid peroxidase autoimmunity				
Positive	15 (44.1)	19 (55.9)	34 (42.5)	0.001
Negative	3 (6.5)	43 (93.5)	46 (57.5)	
Thyroglobulin autoimmunity				
Positive	14 (38.9)	22 (61.1)	36 (45.0)	0.001
Negative	4 (9.1)	40 (90.9)	44 (55.0)	

Abbreviations: BMI, body mass index; TSH, thyroid-stimulating hormone.
[a]Hypothyroid: defined as TSH value > 5.5 mIU/L.
[b]Euthyroid: defined as TSH level between 0.5 and 5.5 mIU/L.

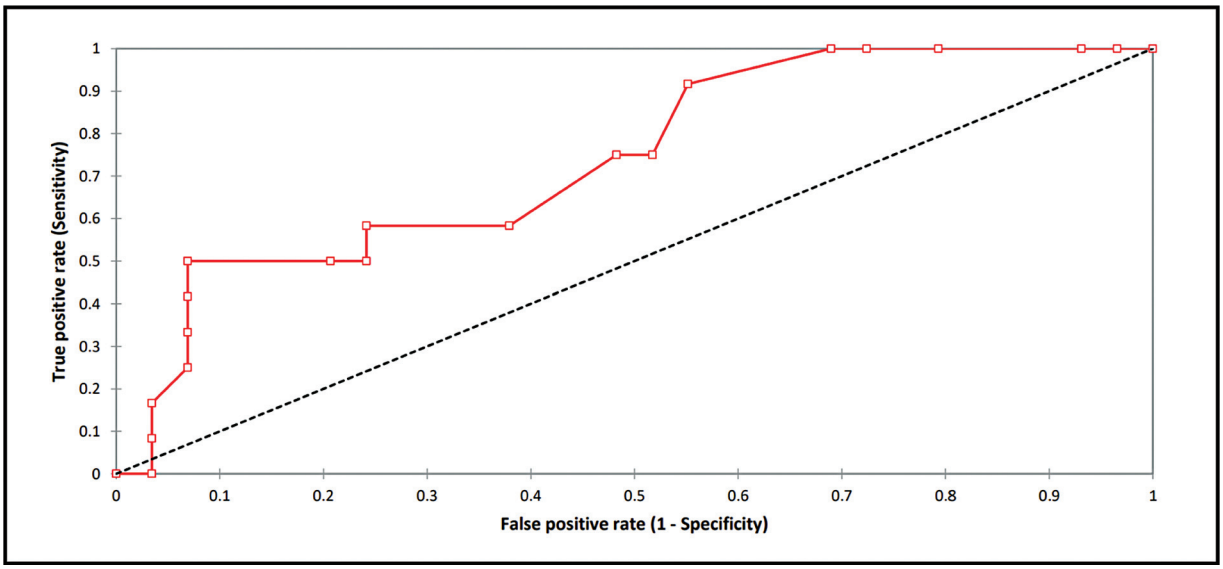

Fig. 1 Receiver operating characteristic curve for preoperative thyroid-stimulating hormone level in predicting postlobectomy hypothyroidism.

lobectomy, 21.1% of people developed hypothyroidism.[11] The pooled risk of hypothyroidism after lobectomy from 22 studies on meta-analysis conducted by Verloop et al was 22%.[9] On the other hand, Lang et al's study reported a higher incidence of hypothyroidism, as they noticed that 29.3% of participants had postoperative hypothyroidism, and one-third of them needed thyroxine replacement.[16] The incidence of postlobectomy hypothyroidism in the Ng et al study was 13%, at the lower end of the reported incidence quoted in the literature.[17] Hypothyroidism has a broad spectrum of presentations ranging from asymptomatic to severely symptomatic.[18] Therefore, surgical decision should be made after judicious balance between the primary surgical indication and the possibility of developing hypothyroidism postoperatively.

Lifelong medication and regular medical follow-up can greatly affect patients' quality of life. Thus, predicting risk factors for developing hypothyroidism after partial thyroid surgery is essential.[19] Some risk-scoring systems have been described to predict hypothyroidism after lobectomy. However, most of these have only one variable or are applicable after surgery, making them difficult to use in preoperative predictions.[20] Many studies have proposed risk factors for developing postlobectomy hypothyroidism, like higher preoperative TSH, the presence of antithyroid antibody and lymphocytic infiltration of the gland, higher resected lobe size, and lower remaining thyroid volume. Nevertheless, these risk factors are not the subject of a clear consensus in the literature.[8]

This study found no significant associations between patient age, sex, BMI level, histopathology, and surgical approach with the development of postoperative hypothyroidism. A recent study by Meyer et al revealed that postlobectomy hypothyroidism and thyroxine replacement were significantly associated with older age and malignant thyroid pathology. No correlation existed with sex, BMI, and family history ($p > 0.05$).[6] In the same concern, Cho et al study found that age, sex, follow-up period, and operation type performed were not significant factors for postlobectomy hypothyroidism development.[11]

This study observed that the mean preoperative TSH level was significantly higher in patients who developed postlobectomy hypothyroidism ($p = 0.001$).

Moreover, ROC curve analysis reported that preoperative TSH level more than 2.61 mIU/L is the best predictor for postlobectomy hypothyroidism. Preoperative TSH level was 60% sensitive and 89.7% specific for that purpose. With a cutoff value of 2.0 mIU/L, the Cho et al study found that the proportion of postlobectomy hypothyroidism was significant in individuals with high-normal preoperative TSH levels.[11] Similarly, Park et al reported that preoperative TSH levels differed significantly between patients with postoperative hypothyroidism and those with postoperative euthyroidism,[20] which agreed with the results of other studies like Lang et al in which hypothyroidism was associated with a higher preoperative TSH level and Meyer et al which report that postlumpectomy hypothyroidism was associated with a higher preoperative TSH.[6,16]

Subclinical thyroiditis can be detected through increased autoantibodies preoperatively.[11] This study proves that thyroid autoimmunity is a valuable predictor of postoperative hypothyroidism. Thyroid peroxidase has 83.3% sensitivity and 69.4% specificity, while slightly lower values have been estimated for thyroglobulin autoantibodies sensitivity of 77.8% and specificity of 64.5%. Furthermore, the combination of TPO and thyroglobulin antibodies in the same patient increases the sensitivity to 100% and specificity to 98.4% to predict future thyroid failure. Similarly, Cho et al reported that the incidence of postlobectomy hypothyroidism is significantly higher in those with two or more positivity on preoperative thyroglobulin, ATA, and antimicrosomal antibody ($p = 0.006$, odds ratio = 9.492). It was significant at 67% sensitivity and 83% specificity to predict postlobectomy hypothyroidism.[11]

Table 3 Diagnostic accuracy of preoperative TSH and autoimmune markers as a predictor for risk of postlobectomy hypothyroidism

Marker	Sensitivity	Specificity	PPV	NPV	Accuracy
Preoperative TSH level (m IU/L)	60%	89.7%	65%	81.4%	75.6%
Thyroid peroxidase autoimmunity	83.3%	69.4%	44.1%	93.5%	72.5%
Thyroglobulin autoimmunity	77.8%	64.5%	38.9%	90.9%	67.5%
Combined thyroid peroxidase and thyroglobulin autoimmunity	100%	98.4	94.7%	100%	98.8%

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; TSH, thyroid-stimulating hormone.

The predictive value of screening tests of postoperative hypothyroidism can be enhanced by finding multiple risk factors in the same individual as compared to either one alone.[21] Therefore, good preoperative evaluation is very important to ensure good thyroid outcome after surgery.

Conclusion

Higher TSH levels and thyroid autoimmunity predict a higher risk of developing hypothyroidism after thyroid lobectomy. Good preoperative evaluation is necessary to predict postoperative thyroid outcome. Surgical decision should be made after proper balance between surgical indication and the possibility to develop hypothyroidism in the future.

Compliance with Ethical Principles

The study was approved by the ethical committee at Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) and Zain Alabdeen Teaching Hospital, Basrah, Iraq.

Authors' Contributions

S.S.T. collected data, performed statistics, and drafted the manuscript. A.M.S.A. guided the study, collected data, and supervised the work. Q.B.J.Al-Z. guided the study, collected data, and supervised the work. A.A.M. designed the study and supervised the work.

Funding and Sponsorship

None.

Conflict of Interest

None declared.

References

1 Latoo MA, Jallu AS, Batool Qurat-ul-ain. Postoperative hypothyroidism after lobectomy for colloid goiter. OTO Open 2021;12 (02):21–24
2 Keestra S, Högqvist Tabor V, Alvergne A. Reinterpreting patterns of variation in human thyroid function: an evolutionary ecology perspective. Evol Med Public Health 2020;9(01): 93–112
3 Machens A, Lorenz K, Dralle H. Peak incidence of pheochromocytoma and primary hyperparathyroidism in multiple endocrine neoplasia 2: need for age-adjusted biochemical screening. J Clin Endocrinol Metab 2013;98(02):E336–E345
4 Park S, Jeon MJ, Song E, et al. Clinical features of early and late postoperative hypothyroidism after lobectomy. J Clin Endocrinol Metab 2017;102(04):1317–1324
5 Lee DY, Seok J, Jeong WJ, Ahn SH. Prediction of thyroid hormone supplementation after thyroid lobectomy. J Surg Res 2015;193 (01):273–278
6 Meyer C, Anderson D, Dong Z, Riddick JB, Elrod M, Ayala M. Prediction of thyroid hormone replacement following thyroid lobectomy: a long-term retrospective study. OTO Open 2021;5 (01):2473974 × 21992001
7 Said M, Chiu V, Haigh PI. Hypothyroidism after hemithyroidectomy. World J Surg 2013;37(12):2839–2844
8 Chong SS, Hoh SY, Huang SM. Post-hemithyroidectomy hypothyroidism in non autoimmune thyroiditis patients: incidence, risk factors and duration of follow up. Asian J Surg 2019;42(11): 957–962
9 Verloop H, Louwerens M, Schoones JW, Kievit J, Smit JW, Dekkers OM. Risk of hypothyroidism following hemithyroidectomy: systematic review and meta-analysis of prognostic studies. J Clin Endocrinol Metab 2012;97(07):2243–2255
10 Miller FR, Paulson D, Prihoda TJ, Otto RA. Risk factors for the development of hypothyroidism after hemithyroidectomy. Arch Otolaryngol Head Neck Surg 2006;132(01):36–38
11 Cho JS, Shin SH, Song YJ, et al. Is it possible to predict hypothyroidism after thyroid lobectomy through thyrotropin, thyroglobulin, anti-thyroglobulin, and anti-microsomal antibody? J Korean Surg Soc 2011;81(06):380–386
12 Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26(01):1–133
13 Kim J, Park HK, Ha T. Predictors associated with the maintenance of normal thyroid function after unilateral total thyroidectomy in patients with papillary thyroid microcarcinoma. J Endocr Surg. 2019;19(03):51–58
14 Ahn D, Sohn JH, Jeon JH. Hypothyroidism following hemithyroidectomy: incidence, risk factors, and clinical characteristics. J Clin Endocrinol Metab 2016;101(04):1429–1436
15 Elmas F, Lauber F, Linder T, Müller W. [Hypothyreosis after Hemithyroidectomy - surprisingly frequent complication in aftercare]. Laryngorhinootologie 2018;97(01):24–29
16 Lang BH, Wong CKH, Wong KP, Chu KK, Shek TWH. Effect of thyroid remnant volume on the risk of hypothyroidism after hemithyroidectomy: a prospective study. Ann Surg Oncol 2017; 24(06):1525–1532
17 Ng P, Ho C, Tan WB, et al. Predictors of thyroxine replacement following hemithyroidectomy in a south east Asian cohort. Head Neck 2019;41(05):1463–1467
18 Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet 2017;390(10101):1550–1562
19 Jonklaas J, Bianco AC, Bauer AJ, et al; American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for

the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. Thyroid 2014;24(12):1670–1751

20 Park HK, Kim DW, Ha TK, et al. Factors associated with postoperative hypothyroidism after lobectomy in papillary thyroid microcarcinoma patients. Endocr Res 2015;40(01):49–53

21 Lee J, Youn W. Hypothyroidism After Hemithyroidectomy: Incidence, Risk Factors, Natural History and Management [Internet]. Hypothyroidism - Influences and Treatments. InTech; 2012. Accessed June 12, 2023 at: http://dx.doi.org/10.5772/32153

