

## Original Article

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# Evaluation of Post-Hemithyroidectomy hypothyroidism

S. M. Abdul Awual<sup>1</sup>, Syeda Marufa Hasan<sup>2</sup>, Suhel Al Muzahid Reza<sup>3</sup>, Md. Shahriar Islam<sup>4</sup>, Utpaul Kumar Sarkar<sup>5</sup>, Md. Abul Kashem<sup>6</sup>

### Abstract:

**Objective:** To evaluate the incidence of post-hemithyroidectomy hypothyroidism and identify possible risk factors that indicates which patients require thyroid function monitoring after surgery.

**Methods:** A prospective study of patients with benign, non-toxic thyroid disease undergoing hemithyroidectomy between January 2017 and July 2019 in the Department of Otolaryngology and Head-Neck Surgery, Sir Salimullah Medical College Mitford Hospital, Dhaka. All patients were in euthyroid state preoperatively. Thyroid specimens were examined for pathological diagnosis and thyroid function was evaluated again six weeks after surgery.

**Results:** All had normal preoperative thyroid function. Six weeks after surgery, 10 (22.22%) of the cases developed hypothyroidism (6.66% overt or symptomatic hypothyroidism and 15.56% subclinical hypothyroidism). The mean preoperative TSH level was significantly higher in the hypothyroid group than in the euthyroid group ( $2.1 \pm 1.1$  vs  $1.3 \pm 0.7$  mIU/L,  $p < 0.01$ ). Seven of patients with preoperative thyroid stimulating hormone (TSH) level more than or equal to 2 mIU/L developed hypothyroidism in comparison to only 3 of those with preoperative TSH  $< 2$  mIU/L (odds ratio 11.3).

**Conclusion:** Ten (22.22%) patients in the present study developed hypothyroidism after hemithyroidectomy. Preoperative TSH more than or equal 2 mIU/L, elevation of thyroid antibodies and thyroiditis warrant post-operative close TSH monitoring. Awareness of such risk factors for post-operative hypothyroidism would improve patients care and reduce complications.

**Keywords:** Hemithyroidectomy, Hypothyroidism, Risk factors.

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1. Assistant Professor (ENT), Sir Salimullah Medical College, Dhaka.
  2. Assistant Professor (Biochemistry), National Institute of Laboratory Medicine and Referral Center, Dhaka.
  3. Assistant Professor (Urology), Sheikh Hasina Medical College, Tangail.
  4. Registrar (ENT), Sir Salimullah Medical College Mitford Hospital, Dhaka.
  5. Assistant Registrar (ENT), Sir Salimullah Medical College Mitford Hospital, Dhaka.
  6. Assistant Registrar (ENT), Sir Salimullah Medical College Mitford Hospital, Dhaka.

**Address for Correspondence:** Dr. S. M. Abdul Awual, Assistant Professor (ENT), Sir Salimullah Medical College, Dhaka. Email: smabdulawual@gmail.com

**Introduction:**

Thyroid is an endocrine gland which is responsible for our normal growth, development and metabolism<sup>1</sup>. Thyroidectomy is performed for various thyroid condition in all over the world and hemithyroidectomy is one of them. Hemithyroidectomy is considered an adequate treatment for several thyroid diseases such as unilateral goiter, toxic adenoma, follicular neoplasm and some suspected malignancies. Theoretically hemithyroidectomy preserves sufficient functioning native thyroid tissue for patients to keep euthyroid status postoperatively without the need for thyroid hormone replacement. But in some patients who have undergone hemithyroidectomy will require thyroid hormone replacement because they have developed hypothyroidism. During the post-operative follow up this hypothyroidism is commonly diagnosed with the help of elevated levels of Thyroid Stimulating Hormone (TSH). Although there is a transient feedback response of pituitary gland to raise serum TSH to induce hyperplasia of the residual thyroid gland immediately after thyroid surgery, this usually returns to normal level within six to 12 weeks.<sup>2,3,6-8</sup>

The incidence and risk of hypothyroidism in patients undergoing hemithyroidectomy remains unclear. Several studies about thyroid function after hemithyroidectomy for benign thyroid disease have been published. The incidence of hypothyroidism in patients undergoing hemithyroidectomy remained inconclusive ranging from 5 to 41.9% and depends on the defined hypothyroidism and its follow-up interval.<sup>2-7,11,12,15</sup> These disparities are a reflection of the variable follow-up and the definition of hypothyroidism used in previous studies. These variations have led to our interest in defining uniform criteria for diagnosis and treatment of

postoperative hypothyroidism, thereby identifying patients at the greatest risk of requiring long-term thyroid hormone replacement.

Routine levothyroxine prescribed for patients after hemithyroidectomy was a common practice in the past to prevent recurrent nodules in the residual thyroid; to decrease risk of malignant conversion in recurrent follicular adenoma, or to treat hypothyroidism, but this concept recently fell out of favor due to its questionable efficacy and associated side effects<sup>2-5, 7, 9</sup>. Patients who developed hypothyroidism following hemithyroidectomy will require life-long thyroid hormone replacement, as well as routine laboratory investigations and medication adjustments. Long-term administration of levothyroxine could cause up to three times higher risk of arrhythmia, atrial fibrillation, or osteoporosis/osteopenia in elderly especially postmenopausal women<sup>3, 5, 6</sup>. The dose of levothyroxine is adjusted on the basis of the result of serum thyroid stimulating hormone (TSH) and thyroxine (T4) levels performed 4 to 6 weeks after the thyroid replacement therapy<sup>11</sup>.

The aim of the present study is to evaluate the incidence of post-hemithyroidectomy hypothyroidism, to identify the possible risks for this condition, and to determine which patients require closed thyroid functions monitoring after surgery.

**Methods:**

A prospective cross-sectional study was carried out among 45 euthyroid patients with benign, non-toxic thyroid disease who had undergone hemithyroidectomy from January 2017 to July 2019 admitted in the Department of Otolaryngology and Head-Neck Surgery, Sir Salimullah Medical College Mitford Hospital, Dhaka.

The patients were selected by adopting purposive sampling techniques with maintaining some inclusion criteria. Before starting the study, we took written informed consent from the study participants. IBM Statistical Package for Social Science (SPSS), version - 22 was used for analyzing collected data.

#### **Inclusion criteria:**

All euthyroid patients, who underwent hemithyroidectomy operation during the study period aged between 15 to 70 years.

#### **Exclusion criteria:**

The patients with preoperative abnormal thyroid function tests, thyroid carcinoma, previous radioactive iodine treatment, or radiation therapy in the head and neck region, or taking medications that might affect thyroid functions such as contraceptive pills or thyroid hormone, critically ill patients and if patients were not interested to include the study.

#### **Study Procedure:**

All recruited patients had serum FT3, FT4, and TSH measured and were in euthyroid state preoperatively. In some suspected patients, preoperative serums anti-Thyroid Peroxidase Antibody (Anti TPO-Ab) also analyzed. All thyroid specimens were examined histologically. A post-operative thyroid function test was performed six weeks after thyroid surgery in all patients. All patients with elevated TSH should also be evaluated for clinical symptoms of hypothyroidism such as exhaustion, generalized edema, weight gain, muscle pain, constipation, and cold intolerance, and correlated to their serum FT3, FT4, and TSH.

Hypothyroidism was classified as subclinical and overt type on the basis of TSH, FT3, and FT4 level. The reference range for normal TSH assay measured in the present study was 0.3 - 5.0 mIU/L; for FT3, 2.80 - 9.50 pmol/L; for FT4, 9.50 - 25.50 pmol/L. Patients with

TSH >5 mIU/L and low FT3, FT4 were classified as overt hypothyroidism. Subclinical hypothyroidism was defined with TSH >5 with normal FT3, FT4 level. Thyroxine replacement therapy was recommended only in patients with overt or subclinical hypothyroidism with symptoms. Subclinical hypothyroidism patients without symptoms should have serial TSH monitoring to detect ongoing overt hypothyroidism.

#### **Data analysis:**

The IBM software SPSS22 was used for statistical analysis in this study. All continuous data were presented as mean and standard deviation; unpaired t-test was used to compare two different means. Frequency and percentage were represented those categorical data and Chi-square test or The Fisher's exact test or Odd ratio was used to determine the difference between each category. A *p*-value <0.05 was considered as statistically significant.

#### **Results:**

Forty-five patients who obtained hemithyroidectomy in the Department of Otolaryngology and Head-Neck Surgery, Sir Salimullah Medical College Mitford Hospital between January 2017 to June 2019, and met the eligible criteria were recruited for the present study. Forty patients were female and five were male. The mean age was  $32.36 \pm 11.53$  years (range 17-65 years).

**Table-I :**  
*Age distribution of patients*

Age	Hypothyroid group	Euthyroid group	Total
<20 years	1	3	4
21 – 30 years	3	17	20
31 – 40 years	4	8	12
41 – 50 years	1	5	6
> 50	1	2	3
Total	10	35	45

Twenty-four thyroid nodules were located on the right side of the neck, 21 were located on the left. The size of thyroid nodules ranged from 2 to 7 cm (mean size  $3.4 \pm 1.2$  cm). All recruited patients had normal preoperative thyroid function.

**Table - II :**  
*Sex distribution of patients*

Sex	Hypothyroid group	Euthyroid group	Total
Male	2	3	5
Female	8	32	40
Total	10	35	45

Preoperative Anti-Thyroid Peroxidase (TPO) antibody test was performed in 18 suspected patients and 15 cases had negative ratio, but all of the 3 patients with positive ratio developed hypothyroidism.

**Table - III :**  
*Preoperative Anti-Thyroid Peroxidase (TPO) antibody report of patients. n=18*

Anti- TPO antibody	Hypothyroid group	Euthyroid group	Total
Normal	4	11	15
Raised	3	0	3
Total	7	11	18

The histopathological report after surgery included 25 cases of nodular goiter, 17 follicular adenoma, and 3 chronic lymphocytic thyroiditis. Histopathological types have no statistical relation with hypothyroidism.

**Table IV :**  
*Histopathological report of patients.*

Histopath- ological type	Hypothyroid group	Euthyroid group	Total
Nodular goiter	5	20	25
Follicular adenoma	3	14	17
Lymphocytic thyroiditis	2	1	3
Total	10	35	45

After the end of the first 6-week post-operative visit, thyroid function test was done and overt or symptomatic hypothyroidism was detected in 3 (6.66%) cases, whereas subclinical hypothyroidism was found in 7 (15.56%) cases. Therefore, the overall prevalence of post-hemithyroidectomy hypothyroidism in the present study was 10 (22.22%).

**Table-V:**  
*Pre-operative Serum TSH level (mIU/L).*

Serum TSH level	Hypothyroid group	Euthyroid group	Total
$\geq 2$ mIU/L	7	6	13
$< 2$ mIU/L	3	29	32
Total	10	35	45

Odds Ratio (OR) is 11.3 (95% CI 2.247 - 56.594). This means that the patients who have TSH level  $> 2$  mIU/L are 11.3 times more risk of developing hypothyroidism than those who have TSH  $< 2$  mIU/L.

**Table -VI :**  
*Average Pre and Post-operative Serum TSH level (mIU/L).*

Serum TSH level	Hypothyroid group	Euthyroid group
Preoperative (Mean $\pm$ SD)	2.1 $\pm$ 1.1	1.3 $\pm$ 0.7
Postoperative (Mean $\pm$ SD)	7.6 $\pm$ 1.5	2.2 $\pm$ 0.9

(*t*-test: 2.1 vs 1.3 mIU/L,  $p < 0.01$ )

### Discussion:

Development of hypothyroidism has been an obvious effect after total, near total, or subtotal thyroidectomy; however, it recently becomes increasing concerns for the patient after hemithyroidectomy. The incidence of hypothyroidism in patients undergoing hemithyroidectomy remained inconclusive ranging from 5 to 41.9% and depends on the defined hypothyroidism and its follow-up interval<sup>11,12,15</sup>. Most patients with hypothyroidism after surgery would develop sign or symptoms within six months. In fact, the half-life of thyroxine that was produced by thyroid gland is seven days and we should allow four to five half-life of thyroxine to get an accurate assessment of the residual thyroid lobe capacity. Therefore, the optimal time for post-operative TSH evaluation should start beyond six weeks<sup>2,3,6,12,11</sup>. In our study, by post-operative 6-week serum TSH evaluation, hypothyroidism could be detected in 22.22% of the cases and overt hypothyroidism was found in 6.66% (treated by thyroxine replacement).

There are many contributing factors had been related to increasing risk of hypothyroidism after thyroidlobectomy such as age, sex, multinodular goiter, preoperative serum TSH, circulating thyroid antibodies (anti-microsomal and thyroglobulin antibodies) and the degree of lymphocytic infiltration in the resected thyroid<sup>4,6-8,11</sup>. Our study confirmed that only preoperative high normal serum TSH, abnormal Anti-Thyroid Peroxidase (TPO) antibody, histologic thyroiditis in the resected gland could predict this complication.

Serum TSH level in the upper end of the normal laboratory range in many studies has been emphasized as a sensitive indicator to predict subsequent development of hypothyroidism. The higher TSH levels may indicate the relatively decrease in both

quantitative and qualitative thyroid reserve but hypothyroidism after this condition is rarely progressive and usually mild in nature<sup>6</sup>. Hypothyroid patients tended to have higher preoperative TSH level when compared to those euthyroid patients; and our finding was similar with others. The mean preoperative serum TSH level in our hypothyroid group was significantly higher than those in the euthyroid groups (2.1 vs 1.3 mIU/L,  $p < 0.01$ ). The patients who have TSH level  $> 2$  mIU/L are 11.3 times higher risk of developing hypothyroidism than those who have TSH  $< 2$  mIU/L (OR=11.3, 95% CI 2.2 - 56.6).

Autoimmune thyroiditis is the end result of inflammatory process by thyroid antigen and its antibody, which could be predicted preoperatively through serum Thyroid microsomal antibody (TMA) and Antithyroglobulin antibody (TGA) in addition to fine needle aspiration finding<sup>16</sup>. Thyroiditis is the most common cause of spontaneous hypothyroidism and it has a trend towards long-term hypothyroidism by progressive tissue destruction from this chronic inflammation. Although TMA (TPO-Ab) and TGA could predict hypothyroidism preoperatively, it could also be found up to 7% in normal population and TGA was found to be less relevant than TMA in detecting thyroiditis. Therefore, histologic thyroiditis does not necessarily correlate with the level of circulatory antibodies (serologic thyroiditis) in all cases<sup>6</sup>. However, only three patients in this study had mild elevation of anti TPO Antibody levels preoperatively and all them were hypothyroid in post-operative period.

There is no universally accepted guideline for post-thyroid lobectomy thyroid function monitoring<sup>4,17,18</sup>. For patients who had preoperative low normal TSH or non-thyroiditis and the first visit (6 weeks) had normal TSH result, thyroid function might be monitored every six months for the first year and on a yearly basis thereafter, since it is

rarely developing hypothyroidism. However, patients with normal TSH level at the first post-operative visit but with numerous risk backgrounds such as preoperative high normal serum TSH, elevated thyroid antibodies titers, or thyroiditis in the resected thyroid, should have serum TSH monitoring follow-ups that include scheduled serial TSH draws at 3, 6, 12 months and on a yearly basis post-operatively to detect the possible late development of hypothyroidism<sup>4,12,19</sup>.

There is a standard care to treat overt hypothyroid patients with thyroxine replacement therapy. Periodic serum TSH evaluation during the follow-up period may guide the dose adjustment. Many investigators had suggested a wait-and-see policy to patients with subclinical hypothyroidism especially those with preoperative high normal serum TSH without other risk factors since this condition is rarely progressive and up to 70% of the cases will recover normal function without any intervention<sup>3,6,8,13,16,17</sup>. In these patients, serum TSH should be monitored every six months until it reaches normal level or patients develop symptoms. However, long-term observation of persistent subclinical hypothyroidism in those chronic thyroiditis patients is associated with left ventricular hypertrophy, unfavorable lipid profile, and increased risk of developing a major depressive or mood disorder. Therefore, early low dose thyroxine replacement in this group could reduce the complications<sup>4,16,19</sup>.

#### **Conclusion:**

Over a one fifth of the patients in the present study (22.22%) developed hypothyroidism after hemithyroidectomy. Preoperative high normal TSH(>2mIU/L) or elevation of thyroid antibodies, the presence of thyroiditis on histology warrant post-operative TSH close monitoring. The awareness to identify such

risk factors for developing hypothyroidism would improve management strategy and better patient care. Thyroxine replacement therapy should be applied only to that overt or symptomatic hypothyroidism, in patients with subclinical hypothyroidism, some could be carefully observed without replacement.

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