



ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE
DEPARTMENT OF SURGERY

Research Title

Rate of hypothyroidism and its clinical predictors in patients with thyroid disorders undergoing Hemi-thyroidectomy and Subtotal thyroidectomy: A retrospective Cross-sectional study from Ethiopia

Investigator:

Tesfaye Aga, MD, General Surgeon, EBS Fellow

tesfaye.aga@aau.edu.et

Advisor:

Endale Anberber, MD, General, Endocrine and Breast Surgeon

Endale.anberber@yahoo.com

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ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publications Office in effect at the time of Grant is forwarded as the result of this application.

Name of the student:

DR. TESFAYE AGA DINAGDE _____

Signature _____ Date _____

APPROVAL FORMS OF ADVISOR

Name of the advisor:

DR. ENDALE ANBERBER _____

Signature _____ Date _____

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ABSTRACT

Introduction: Hypothyroidism is one the most frequently encountered complications following thyroidectomy. Thyroidectomy results in deranged function of the thyroid gland, which corresponds to the extent of resection. The risk of hypothyroidism after thyroid surgery varies in different studies. Hemithyroidectomy and subtotal thyroidectomy are associated with up to 10 to 50% and 50-84% of hypothyroidism respectively. Factors like, old age, type of surgery, pathologic diagnosis, lymphocytic infiltration, elevated preoperative TSH level, use of levothyroxine before surgery and preoperative detectable anti-TPO antibody are associated with the increased incidence of hypothyroidism. This study, which is the first of its kind in our country, aims to assess the incidence and predictors of hypothyroidism following thyroid surgery

Objectives: To assess the incidence of hypothyroidism after thyroidectomy and predictors for the development of hypothyroidism.

Methodology: A descriptive cross-sectional study was conducted on patients who underwent hemi-thyroidectomy or STT for various thyroid pathologies at Lancet General Hospital and Tikur Anbessa Specialized Hospital from January 1, 2021 to December 31, 2024. Source of data was the patient's medical record. The study variables required filled on a structured data collection tool which was then entered into SPSS software and interpreted. Ethical approval was obtained from the research committee (IRB) of Addis Ababa University, College of health sciences, School of medicine.

Result: A total of 102 patients in the age range of 18-70 years were studied. 78 females (76%) and 24 males (24%) with median age of 43 years were included. Median age of females is 43 years and median age of males is 46 years. Six weeks

post-surgery, hypothyroidism was diagnosed in 24.6% of patients with hemi-thyroidectomy and in 38% of patients with subtotal thyroidectomy. in those patients who had follow up at 6-month months post-surgery, hypothyroidism was diagnosed in 23% of patients with hemi-thyroidectomy and in 29% of patients with subtotal thyroidectomy.

Conclusion: There is high prevalence of hypothyroidism in post-thyroidectomy patients in our center which is more or less comparable to studies in the rest of the world. In this study, the overall incidence of hypothyroidism after non-total thyroidectomy is 29% and 26% at 6 weeks and 6 months post-surgery, respectively.

Key words:

Hemithyroidectomy, Hypothyroidism, Sub-total thyroidectomy,

Post-surgery

ABBREVIATIONS

BL-STT: Bilateral Subtotal Thyroidectomy

GD: Grave's Disease

HT: Hemi-thyroidectomy

IRB: Institutional review board

MNG: Multinodular Goiter

MRN: Medical Record number

NTT: Near Total Thyroidectomy

OR: Operation room

PI: Principal Investigator

PTMC: Papillary Thyroid Microcarcinoma

PTU: Propylthiouracil

SPSS: Statistical package for social sciences

STT: Subtotal Thyroidectomy

T3: Tri-iodothyronine

T4: Thyroxine

TSH: Thyroid Stimulating Hormone

TPO: Tyrosine Peroxidase

TT: Total Thyroidectomy

UTL: Unilateral Thyroid Lobectomy

INTRODUCTION

Background

Thyroidectomy is one of the most frequently performed surgeries worldwide and Ethiopia in particular, of which partial and subtotal thyroidectomy are the most commonly performed types of thyroid operation(1). Hypothyroidism is one the most frequently encountered complications following thyroidectomy. Hypothyroidism is defined as thyroid hormone deficiency in the body. Autoimmune thyroiditis and iatrogenic mechanisms such as radioactive iodine therapy and thyroidectomy are the most common causes of hypothyroidism(2). Thyroid surgery, by its nature, alters thyroid gland function proportionally to the amount of tissue removed. This altered function can manifest as changes in hormone levels (biochemical), clinical symptoms, or both. Biochemical changes, detectable through TSH, T4, and T3 blood tests, often precede noticeable clinical symptoms. These hormone assays are the most reliable (gold standard) method for evaluating and predicting thyroid gland function after surgery

Hypothyroidism can lead to various clinical symptoms that negatively affect overall health. Beyond the need for ongoing medical appointments and blood tests, long-term thyroid hormone replacement therapy has been linked to potential complications, including accelerated bone loss, atrial fibrillation, alterations in left ventricular function, and reduced psychological well-being.

Post-surgical hypothyroidism and its incidence have not been fully investigated. The reported risk of hypothyroidism after thyroidectomy varies greatly in the literature. According to previous studies the incidence of hypothyroidism after hemithyroidectomy ranges from 10 to 50%(2–7). The incidence of hypothyroidism after subtotal thyroidectomy ranges from 50-84%(8,9). The most common cause of hypothyroidism after thyroid operation is subtotal resection for Grave's disease or

multinodular goiter but autoimmune destruction of the thyroid tissue is another important cause for postoperative hypothyroidism(2). On average one in five patients will develop some form of hypothyroidism after thyroid lobectomy. Although only few studies reported clear data on the distinction between subclinical and clinical hypothyroidism, most of the detected thyroid dysfunction is subclinical hypothyroidism(3).

Following an incomplete or subtotal thyroidectomy, patients are expected to have enough remaining thyroid tissue to restore normal thyroid function within 4-8 weeks as the hypothalamus-pituitary-thyroid axis recovers. Therefore, the development of hypothyroidism suggests a significant delay or failure in this recovery process. The speed, success, or failure of this recovery depends on individual patient factors such as pre-existing health conditions (comorbidities), age, and sex. Moreover, pre-operative levels of thyrotropin (TSH), thyroglobulin (TG), anti-thyroglobulin antibody (ATA), and anti-microsomal antibody (AMA) are all recognized as predictors of postoperative hypothyroidism and influence the recovery trajectory.

Studies have tried to identify factors associated with increased risk of hypothyroidism. Apart from the type of operation, factors such as increased age, operation type, pathologic diagnosis (underlying disease), lymphocytic infiltration, elevated preoperative TSH level, use of levothyroxine before surgery and preoperative detectable anti-TPO antibody are associated with the increased incidence of hypothyroidism (2,3,6,7,11).

Significance of the study

In Ethiopia, there is paucity of data about the incidence of post-thyroidectomy hypothyroidism. To the best of our knowledge there is no published study on this

subject matter. This study aimed to assess the incidence and predictors of hypothyroidism following subtotal thyroidectomy or hemi-thyroidectomy.

In our setting many patients come from distant rural communities where qualified medical personnel and competent laboratories are scarce, making frequent monitoring of thyroid status very difficult to ensure. Therefore, we found it very important to identify preoperative predictive factors for post-operative hypothyroidism in our patients so that proper communication and shared decision regarding the treatment options will be made. This helps in establishing adequate monitoring and treatment or supplementation of these high-risk patients.

Literature review

Studies on the incidence and predictors of post thyroidectomy hypothyroidism show variable results, which might be because of the variation in the study setup and methodology they use.

In 2006, Miller et al. from University of Texas did a retrospective analysis of 90 patients for whom hemi-thyroidectomy was done for different thyroid diseases. The aim of the study was to assess the overall incidence of hypothyroidism and identify the risk factors for development of hypothyroidism, at least 8 weeks after hemithyroidectomy. The overall incidence of the development of hypothyroidism after hemi-thyroidectomy was 27%. Risk factors for the development of hypothyroidism include pathologic diagnosis (Hashimoto thyroiditis and multinodular goiter) as well as a high-normal serum thyrotropin level (3.15 mIU/L)(6).

A 2008 study by Lankarani et al. (Iran) followed 102 patients who underwent thyroidectomy for benign thyroid diseases. Thyroid function was assessed every three months for one year post-surgery, with a baseline measurement taken immediately after the operation. The study found that 36 patients (35.2%) developed

hypothyroidism, on average 5 ± 3.2 months after surgery. Increased age, type of surgical procedure, histopathologic findings, underlying thyroid disease, lymphocytic infiltration, and pre-operative levothyroxine use were all identified as factors associated with a higher incidence of hypothyroidism.

Limonard et al. (Netherlands) retrospectively reviewed the outcomes of 62 patients who underwent subtotal thyroidectomy for recurrent Graves' hyperthyroidism between 1992 and 2008 in a study titled "Thyroid Function after Subtotal Thyroidectomy in Patients with Graves' Hyperthyroidism." After a median follow-up of 54.6 months (range 2.1 - 204.2 months), only 6% of patients were euthyroid. A significant majority (84%) developed hypothyroidism, while 10% experienced persistent or recurrent hyperthyroidism. Based on these findings, the authors concluded that subtotal thyroidectomy offers minimal benefit over total thyroidectomy regarding postoperative thyroid function.

A 2012 systematic review and meta-analysis by Verloop et al., encompassing 32 studies, aimed to determine the overall risk of both subclinical and clinical hypothyroidism following hemithyroidectomy, and to identify associated risk factors. The analysis revealed an overall hypothyroidism risk of 22%. Among the studies that differentiated between the two conditions ($n=4$), the estimated risk was 12% for subclinical hypothyroidism and 4% for clinical hypothyroidism. The review also identified pre-operative TSH levels in the higher-normal range and positive anti-TPO antibody status as significant predictors of thyroid failure after surgery.

A 2017 retrospective cohort study by Lin et al. examined the long-term thyroid function outcomes following subtotal thyroidectomy for Graves' hyperthyroidism. The study enrolled 415 consecutive Graves' disease patients who underwent subtotal thyroidectomy between 2005 and 2011, with a median postoperative follow-up of 72 months (range 12-144 months). The results revealed that hypothyroidism

developed in more than half of the patients, and only 19.3% achieved a euthyroid state. Persistent or recurrent hyperthyroidism was observed in 119 patients, representing 28.7% of the cohort. (8).

Kintu-Luwaga et al. from Uganda, reported a prospective cohort study of 40 patients with the aim to assess the prevalence and pattern of sub-clinical dysthyroidism following thyroid surgery. Subtotal thyroidectomy was the most frequently performed type of surgery (55%). 22.7% of patients who underwent subtotal thyroidectomy had dysthyroidism, the commonest of which is hypothyroidism(10).

Kim et al. from Korea, with a goal to identify factors affecting the maintenance of normal thyroid function after unilateral thyroid lobectomy (UTL) for papillary thyroid microcarcinoma (PTMC), retrospectively analyzed 192 patients from January 2015 and December 2017. Ninety-five (49.5%) patients developed postoperative hypothyroidism. Female sex and increased preoperative TSH levels (cut off= 1.89 mIU/L.) were identified as independent predictors of the development of postoperative hypothyroidism. Based on their observation, they emphasized the need for proper discussion on the potential risk of postoperative hypothyroidism in patients exhibiting elevated TSH levels before initiating surgery(7).

Bakiri et al. (Algeria) conducted a 6-month postoperative study to assess thyroid remnant function and sonographic appearance in 119 patients who underwent subtotal thyroidectomy (STT) for benign multinodular goiter. The surgical outcomes were evaluated using thyroid-stimulating hormone (TSH) assays and cervical ultrasound. The study found an inverse correlation between TSH levels and thyroid remnant volumes. Sonographically, 47 patients exhibited hypoechoic thyroid remnants, while 72 had isoechoic remnants. While no predictive factor was identified for the development of the hypoechoic feature, a strong association was

observed between remnant appearance and TSH levels. Specifically, 97.9% (46/47) of patients with a hypoechoic remnant had TSH levels exceeding 5 mU/L, compared to 54.2% (39/72) of patients with an isoechoic remnant. These results indicate that, following STT for benign multinodular goiter, postoperative hypothyroidism is not solely determined by the volume of the thyroid remnant. The hypoechoic appearance of the remnant on ultrasound is also a significant predictive factor, suggesting that postoperative hypothyroidism may result from either insufficient remnant tissue or the development of a secondary lesion leading to the hypoechoic appearance.

OBJECTIVES

General objectives

To assess the magnitude and predictors of hypothyroidism after STT or Hemithyroidectomy

Specific objectives

To assess the incidence of hypothyroidism after STT and Hemithyroidectomy

To identify predictors for the development of hypothyroidism

MATERIALS AND METHODS

Study design and setting

This is a hospital based retrospective study that done in two specialized hospitals (TASH and LGH) in Ethiopia. TASH is a prominent comprehensive specialized and teaching public hospital. LGH is one of the private hospitals in Addis Ababa, Ethiopia, which provides various specialty and subspecialty services including endocrine surgery.

Study population

The current study is conducted on patients who underwent Hemithyroidectomy (Lobectomy), Dunhill's procedure (Bilateral subtotal thyroidectomy) during a 4-years period, from January 2021 to December 2024.

During this period, a total of 169 patients were treated with either hemithyroidectomy or Subtotal thyroidectomy for various benign and malignant thyroid disorders. Sixty-two (62) patients were excluded due to lack of documentation of study variables. Five patients, who were started on with TSH suppression were also excluded. Thus, the final study sample consisted of 102 patients who were able to undergo regular postoperative thyroid function tests at least once.

Data analysis

Data for study variables was collected using a well-structured data extraction tool prepared on google forms, which was then converted to Microsoft excel and finally exported to data analysis tool (SPSS). The data was checked for completeness and accuracy before processing and analysis.

The Proposal was approved by the IRB of the university. Given the retrospective nature of this study, informed consent is not mandatory.

OPERATIONAL DEFINITIONS

Total Thyroidectomy (TT): is when the whole thyroid gland is resected out

Near total thyroidectomy (NTT): Where less than three grams of the gland is left behind

STT: Only about 25% of a one lobe left intact

Bilateral subtotal Thyroidectomy:

Dunhill's procedure:

Hemi-thyroidectomy (HT): One lobe along with isthmus is removed

Lobectomy: Where only one lobe is excised. Technically they are similar to hemi-thyroidectomy. Therefore, in this particular study we will use the terms interchangeably.

Clinical hypothyroidism: Elevated TSH levels and low thyroid hormone levels, either T3 or T4 or both.

Subclinical hypothyroidism: above normal TSH levels and thyroid hormone levels within the normal range.

Transient hypothyroidism: Occurs less than 6 months after surgery

Permanent hypothyroidism: Hypothyroidism that persists over 6 months after the surgery.

RESULTS

Demographic and clinical characteristics

A total of 102 patients in the age range of 18-70 years were studied. 78 females (76%) and 24 males (24%) with median age of 43 years were included. Median age of females is 43 years and median age of males is 46 years. Based on clinical (functional) diagnosis, 19 cases of toxic goiter (18.8%), while 82 of the cases were non-toxic (simple) goiters (81.2%).

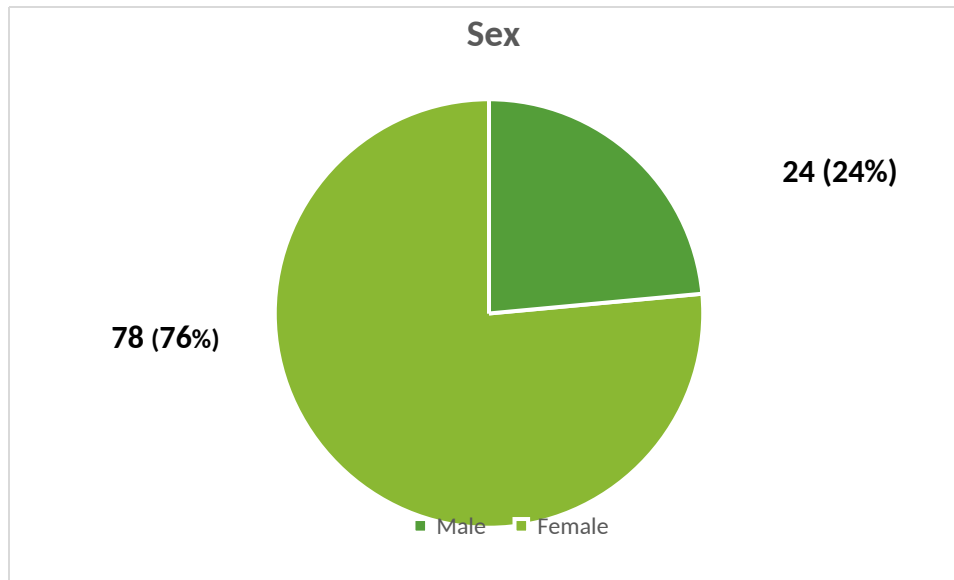


Figure1: Sex distribution of study patients

Morphological feature of the goiter as evidenced by clinical examination and/or sonography findings showed that 55 (54%) of the cases were solitary nodules while 45% of the patients have multinodular goiter. Only 1 patient was operated for diffuse goiter.

Patient characteristics	Median (Range) or Number (Percent)
Age at diagnosis	43 (18-70) years
Sex	
Female	78 (76 %)
Male	24 (24%)
Functional diagnosis	

Simple	82 (81%0
Toxic	19 (19%)
Morphological diagnosis	
MNG	55 (54%)
Solitary nodule	46 (45%)
Diffuse	1(1%)
Surgical indications	
Suspected malignancy	32 (31.7%)
Hyperthyroidism	19 (18.8%)
Patient preference /cosmetics	18 (17.8%)
Retrosternal extension	17 (16.8%)
Pressure symptoms	11 (10.9%)
Recurrence thyroid cyst	1 (1%)
Confirmed malignancy	1 (1%)
Types of surgery	
Hemithyroidectomy/Lobectomy	65 (64%)
Dunhill's thyroidectomy	31 (30%)
Bilateral STT	6 (6%)

Table1: Demographic and Clinical characteristics of study patients

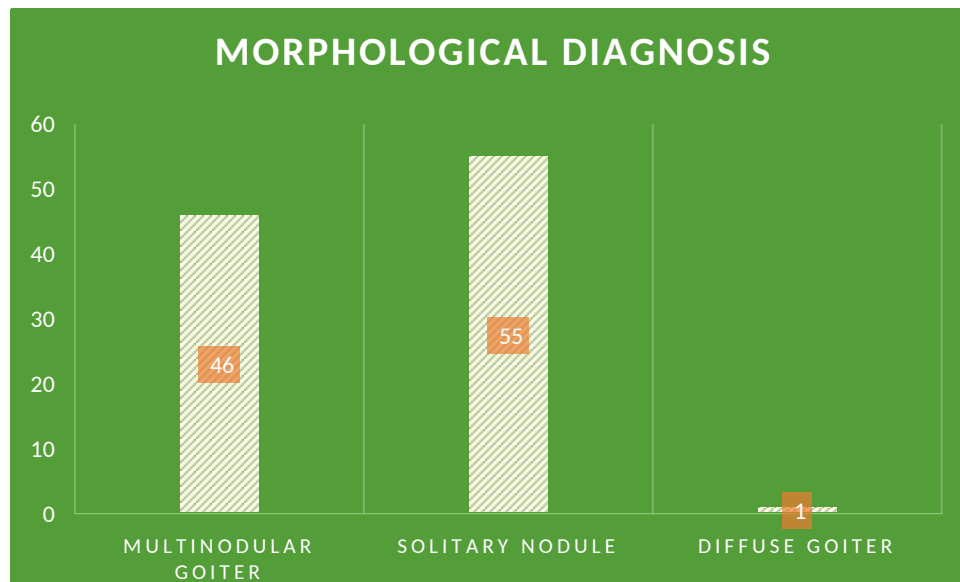


Figure 2: Morphological diagnosis

The common indications for surgery were suspected malignancy (31.7%), patient preference for cosmetic reasons (18.8%), hyperthyroidism (17.8%), retrosternal extension (16.8%) and pressure symptoms (10.9%) among others.

FNAC was done in only 63.7% (65) of the patients. Among them 54% (35 cases) are colloid goiter, 25% (16 cases) are follicular neoplasm, while 12 % (8 cases) are oncocytic neoplasm.

Three types of surgical procedures were used, Hemithyroidectomy (lobectomy-isthmectomy) (65 cases, 63.7%), Dunhill's thyroidectomy (31 cases, 30.4%), and Bilateral Subtotal Thyroidectomy (6 cases, 5.9%).

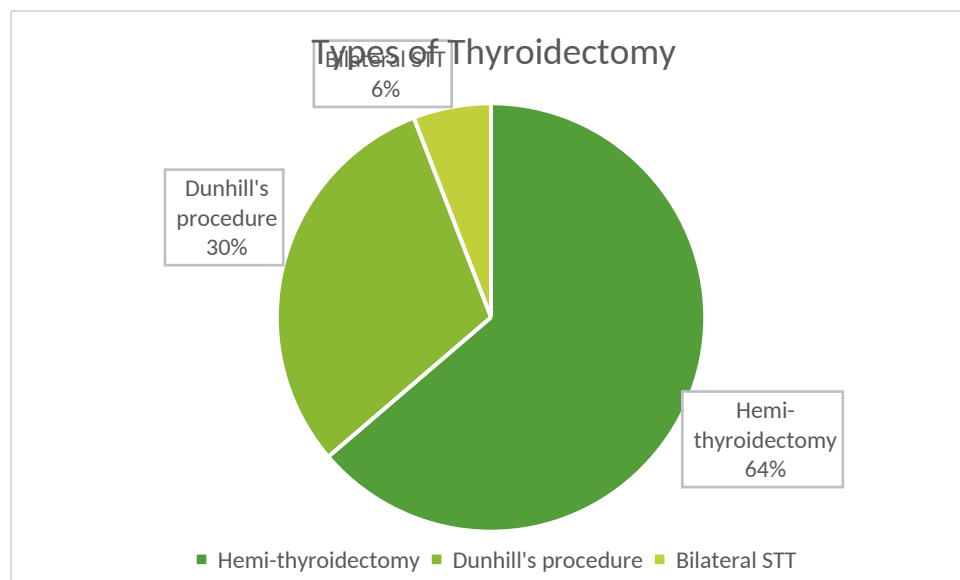


Figure 3: Types of thyroidectomies

One hundred patients have surgical pathology report done. The most common pathologic diagnosis of the patients was nodular colloid goiter (71 cases, 71%), followed by follicular adenoma (12 cases, 12%).

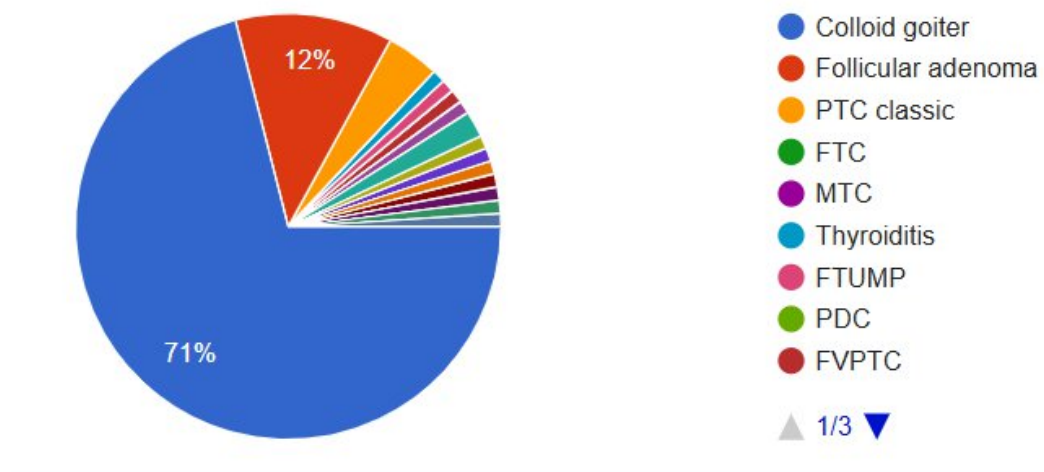


Figure 4: Pathologic diagnosis

Hypothyroidism

On TSH done 6 weeks after the surgery, 29.4% (30 patients) were found to have at Supranormal TSH (at least subclinical hypothyroidism). With regards to the extent surgery, hypothyroidism was diagnosed in 24.6% of patients with hemi-thyroidectomy and in 38% of patients with subtotal thyroidectomy.

Table 1 below shows the percentage of patients who are hypothyroid 6 weeks after surgery with respect to the extent of surgery.

Surgery type	N	Supranormal TSH at 6 weeks	Percent
Hemi-thyroidectomy	65	16	24.6%
Dunhill's procedure	31	11	35.5%
Bilateral STT	6	3	50%
STT (Dunhill's and BL-STT)	37	14	38%

Table 2: Hypothyroidism with respect to the extent of thyroidectomy, 6 weeks post-surgery

At 6 months post-surgery, only 75 patients have their TSH determined. Out of these patients, 26% (19 patients) of the patients have a supranormal TSH level, which is defined as permanent hypothyroidism. With regards to the extent surgery, hypothyroidism was diagnosed in 23% of patients with hemi-thyroidectomy and in 29% of patients with subtotal thyroidectomy.

Surgery type	N	Supranormal TSH at 6 months	Percent
Hemi-thyroidectomy	47	11	23%
Dunhill's procedure	25	6	24%
Bilateral STT	3	2	67%
STT (Dunhill's and BL-STT)	28	8	29%

Table 3: Hypothyroidism with respect to the extent of thyroidectomy, 6 months post-surgery

Author	Country	Sample	Mean age	Type of surgery	Hypothyroidism	
Current study (Tesfaye Aga)	Ethiopia	102	44	HT and STT for various indications	At 6 weeks HT (24.6%) STT (38%)	At 6 months HT (24.6%) STT (38%)
Lankarani et al.	Iran	102	39 ± 13.6	HT and STT for various indications	Time: mean 5 months HT (17.7%), STT (44%)	
Kintu-Luwaga et al.	Uganda	40	44.3	STT	22.7%	
Limonard et al.	Netherland	62		STT for Grave's	Median follow up:	

	s				54.6 months STT (84%)
Lin YS et al.	Taiwan	385	Median 32	STT for Grave's	Median follow up: 70 months STT (50%)
Miller et al.	USA, Texas	90	45	HT	27% (majority in 6 to 12 months)
Verloop et al.	Review and Metanalysi s	32 studie s, 4899	Mean age 37-71	HT for various indications	22% (At various times post-surgery but mostly within 8 weeks)

Table 4: Summary of results from different studies

DISCUSSION

Sample size of our study is one hundred and two (102). Which is adequate as compared to other similar studies (see table 4)

The main goal of doing non-total thyroidectomy and preserving a thyroid tissue is to avoid post procedural hypothyroidism and thereby avoid the need for life long thyroxine supplementation. Patients with non-total thyroidectomy will be hypothyroid in 29 % and 26% at 6 weeks and 6 months respectively.

This study demonstrates that one-quarter (24.6%) of patients with hemi-thyroidectomy and 38% of patients with subtotal thyroidectomy will be hypothyroid at 6 weeks post-surgery, and if we follow them to 6 months 23% of patients with

hemi-thyroidectomy and in 29% of patients with subtotal thyroidectomy will remain in a hypothyroid state.

This finding is similar to results from studies done in Uganda (Kintu-luwaga et al.) and USA (Miller et al.) showed similar incidences of hypothyroidism, while a study by Lankarani et al. from Iran, showed lower incidence of hypothyroidism (17.7%) after hemithyroidectomy and higher rate of hypothyroidism (44%) after STT, five months post-surgery.

Studies done in Taiwan (Lin YS et al.) and Netherlands (Limonard et al.) on patients who had STT for Grave's disease show high incidence of hypothyroidism, which might be due to the long median follow up period and or the underlying pathology (Grave's disease), in these studies.

A systematic review and metanalysis of 32 studies and 4988 patients (Verloop et al.) demonstrated a slightly lower rate (22%) of hypothyroidism after hemithyroidectomy, where majority of the studies use 8 weeks to define hypothyroidism.

CONCLUSION AND RECOMMENDATIONS

Comparable to other similar studies, there is high rate of hypothyroidism in post-thyroidectomy patients in our center. In our study the overall incidence of hypothyroidism after non-total thyroidectomy is 29% and 26% at 6 weeks and 6 months post-surgery, respectively. Longer follow up after surgery may be required to assess the long-term outcome of these patients.

STRENGTHS AND LIMITATIONS

Strengths

As a first study of its kind, it will help as a baseline for further studies on the same subject matter

Limitations

Retrospective nature of the study

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ANNEX

Data collection tool

Thyroid function after hemi-thyroidectomy and subtotal thyroidectomy

A. Socio-demographic characteristics of the patient:

1. MRN: _____
2. Phone number: _____
3. Hospital set-up: _____ a. Public b. Private
4. Age _____
5. Sex: _____ a. Male b. Female
6. Residence: a. Urban b. Rural

B. Clinical data

7. Functional diagnosis?
 - a. Toxic
 - b. Simple
8. Morphological diagnosis
 - a. Multi-nodular goiter
 - b. Solitary nodule
 - c. Diffuse
9. Pathologic Diagnosis
 - a. Neoplastic
 - b. Non-neoplastic
10. Indication for surgery
 - a. Toxicity
 - b. Pressure symptoms
 - c. Cosmetic / Patient preference
 - d. Retrosternal extension
 - e. Suspected or confirmed malignancy

11. For patients with thyrotoxicosis, for how long (months) was she (he) on **antithyroid** drugs? _____
12. What drug (s) was she (he) on? A. PTU b. PTU + propranolol c. Carbimazole d. Carbimazole + propranolol
13. TSH level preoperatively: a. > 5 b. 5-0.5 c. 0.5-0.1 d. < 0.1
14. Interval between diagnosis and surgery? _____
15. Type of Surgery
 - a. Hemithyroidectomy/
 - b. Lobectomy
 - c. Bilateral subtotal thyroidectomy
 - d. Dunhill's procedure
16. Estimated weight or volume of the thyroid remnant (in gm/ml) : _____
17. Estimated weight of the specimen (in gm): _____
18. Pathologic diagnosis:
 - a. colloid goiter
 - b. Thyroiditis
 - c. Follicular adenoma
 - d. PTC
 - e. FTC
 - f. MTC
 - g. Others _____

C. Outcome in TFT

19. TFT at 1 month/ at 6 weeks: a. TSH _____ b. T3 _____ c. FT4 _____
20. Diagnosis: a. Euthyroid b. Subclinical Hypothyroidism c. Clinical Hypothyroidism d. Hyperthyroidism (recurrence)
21. TFT at 6 months: a. TSH _____ b. T3 _____ c. FT4 _____

22.Diagnosis: a. Euthyroid b. Subclinical Hypothyroidism c.
Clinical Hypothyroidism d. Hyperthyroidism (recurrence)