

Original Research Article

A comparative study of postoperative hypocalcaemia following total thyroidectomy in patients with Hashimoto's thyroiditis and multinodular goitre in a rural tertiary care hospital

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ABSTRACT

Background: Recurrent laryngeal nerve injury, hypothyroidism and hypocalcaemia have long been recognized as the three main sequelae of thyroidectomy. Persistent hypocalcaemia may cause intracranial lesions and cardiac arrhythmias. As the definitive diagnosis of Hashimoto's thyroiditis was not always possible with clinical and cytological parameters when antibody testing was not done, surgery was planned with the diagnosis of multinodular goitre. This study was conducted to find out the incidence of post-operative hypocalcaemia following total thyroidectomy by skilled surgeons in patients with multinodular goitre and Hashimoto's thyroiditis.

Methods: This was a cross-sectional study to compare the incidence of hypocalcaemia in patients with biopsy-proven Hashimoto's thyroiditis and multinodular goitre. After obtaining approval from the institutional review board and ethics committee, data was collected serially, from the surgical records of 123 patients who underwent total thyroidectomy in this tertiary care centre, during the past two years.

Results: The incidence of post-operative hypocalcaemia (71.1%) in patients undergoing total thyroidectomy with Hashimoto's thyroiditis was significantly higher than in patients with multinodular goitre (56.4%). Of the 45 patients who had a biopsy report of Hashimoto's thyroiditis, 8 (17.8 %) developed permanent hypocalcaemia while only 8 (10.3%) of the 78 patients with histopathological diagnosis of multinodular goitre developed persistent hypocalcaemia needing supplementation following total thyroidectomy in this rural tertiary care hospital.

Conclusions: The significant risk of post-operative hypocalcaemia should be kept in mind before opting for total thyroidectomy for benign lesions of the thyroid and pre-operative antibody studies must be done to diagnose Hashimoto's thyroiditis.

Keywords: Hashimoto's thyroiditis, Hypocalcaemia, Multinodular goitre, Total thyroidectomy

INTRODUCTION

In surgical endocrinology departments, total thyroidectomy is performed for benign multinodular goitre (MNG) because after subtotal resection of thyroid, rates of up to 40% recurrence has been noted in the long-term follow-up.^{1,2} As early as 1883, complications of thyroidectomy such as recurrent laryngeal nerve injury,

hypothyroidism and hypocalcaemia were recognized as the three main post-operative sequelae of thyroidectomy by Theodore Kocher.³

Hypocalcaemia is a major post-operative complication of total thyroidectomy, causing severe symptoms and increasing hospitalization time.⁴ Transient asymptomatic hypocalcaemia occurs in most patients undergoing

thyroidectomy. Acute symptomatic hypocalcaemia and permanent hypocalcaemia were once quite common with thyroid surgery especially in patients having total thyroidectomy. Rates of these problems have decreased dramatically as the understanding of the anatomy and physiology of the parathyroid glands has increased. Large series of thyroid operations have been reported in which the rates of permanent hypocalcaemia due to hypoparathyroidism are less than 1-2%.⁵

An overwhelming majority of patients with Hashimoto's thyroiditis (HT) with significant symptoms appear to benefit from thyroidectomy and so surgery is often advised for patients with HT for palliation of persistent symptoms after conservative therapy.⁶ However the same researchers have found that there is a higher rate of complications following total thyroidectomy in patients with HT compared to patients without thyroiditis.⁷

Most often the decision to perform total thyroidectomy is based on a clinical or cytological diagnosis which may not differentiate multinodular goitre (MNG) from co-existing Hashimoto's thyroiditis (HT), till the histopathological diagnosis is available. In the absence of antibody testing to diagnose thyroiditis pre-operatively, this study was undertaken to find out if there is a difference in the incidence of post-operative hypocalcaemia following total thyroidectomy by skilled surgeons in patients with a histopathological diagnosis of Hashimoto's thyroiditis compared to multinodular goitre in a rural tertiary care hospital.

METHODS

Ethics committee approval and permissions from institutional authorities were first obtained for this cross-sectional study on 20 January 2017. The medical records of patients who have undergone total thyroidectomy during the period January 2015 to April 2017 were serially accessed from the surgery department of this medical college to collect data for this case series analysis. The objective was to find the incidence of post-operative hypocalcaemia following total thyroidectomy in patients with HT and MNG in this rural tertiary care hospital in South India. All patients above the age of 18 years, who had undergone total thyroidectomy for HT and MNG during the period January 2015 to April 2017 were serially recruited if they fulfilled selection criteria. Patients who had pre-operative hypocalcaemia were excluded. In our study, hypocalcaemia is defined as serum corrected calcium level below 8 mg/dl.⁸

The sample size for single proportion, for a confidence level of 95% and precision of 7.5% was found to be 123 cases. In the observational study by Nair et al hypocalcaemia was diagnosed when serum corrected calcium level dropped below 8 mg/dl. They found the overall incidence of hypocalcaemia in patients who had total thyroidectomy was 23.6%.⁸ The sample size was

calculated by nMaster sample size software by nMaster sample size calculation software.⁹

Regarding standard practice in our institution during the study period, Vitamin D status and bone mineral density were not checked for any of these patients. Thyroid function tests of all the patients were either euthyroid or subclinical hypothyroid. Symptomatic patients were appropriately treated with oral or intravenous calcium supplementation and Vitamin D3.

All the total thyroidectomies included in this study were performed by three skilled surgeons, each of whom has had over five years of experience in performing thyroidectomies, doing at least one surgery per week. In our series no case was done by trainees.

The standard open total thyroidectomy technique, as described in standard textbooks of operative general surgery, were used. After raising the skin flaps we do not use monopolar cautery. All 4 parathyroid glands were identified and were intact in all the cases. In none of the cases these glands were inadvertently removed or required auto-transplantation. The branches of inferior thyroid artery near the inferior parathyroid were dealt with fine vicryl knots and with bipolar cautery only after identifying and securing the recurrent laryngeal nerve and parathyroid glands and taking care to avoid any thermal damage. None of the patients had lymphadenopathy and lymph node dissection was not done for any patient.

The data was entered in a spread sheet and frequencies and percentages were obtained for all variables. The categorical variables were compared using the Chi squared test. The mean values for serum calcium in the two groups were compared using the Student t-test. The methodology of the study is detailed in Figure 1.

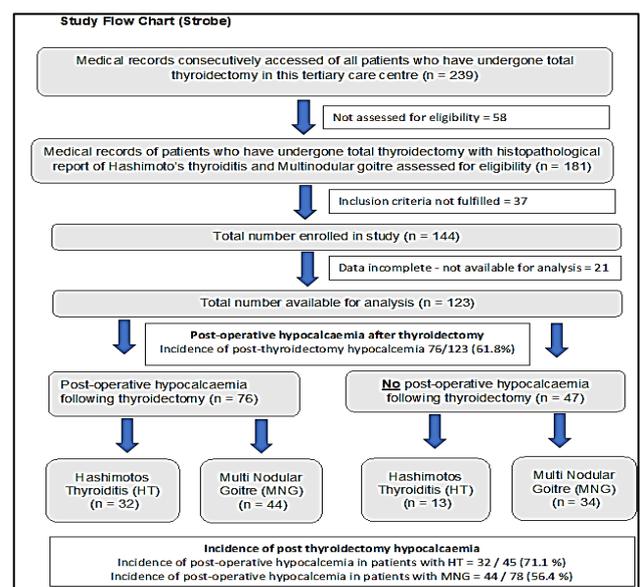


Figure 1: A study of hypocalcaemia following total thyroidectomy for benign conditions.

RESULTS

Of the 239 patients who underwent thyroidectomy in this tertiary care hospital during the study period, 123 were done for benign lesions of the thyroid. Of these the

histopathological diagnosis was Hashimoto’s thyroiditis (HT) in 78 (63.4%) patients and multinodular goitre (MNG) in 45 (36.6%). The baseline characteristics are given in Table 1.

Table 1: Baseline characteristics of patients who underwent total thyroidectomy.

Baseline characteristics		Biopsy diagnosis			P value
		HT (n=45) N (%)	MNG (n=78) N (%)	Total (n=123) N (%)	
Age (in years)	10-29	3 (6.7)	1 (1.3)	4 (3.3)	0.016
	30-49	30 (66.7)	41 (52.6)	71 (57.7)	
	50-69	11 (24.4)	34 (43.6)	45 (36.6)	
	70-89	1 (92.2)	45 (35.6)	3 (2.4)	
Gender	Male	3 (6.7)	12 (15.4)	15 (12.2)	0.088
	Female	42 (93.3)	66 (84.6)	108 (87.8)	
Symptoms	Complaints of swelling in neck	43 (95.6)	77 (98.7)	120 (97.6)	0.255
	Hoarse voice	1 (2.2)	7 (9.0)	8 (6.5)	0.115
	Pressure symptoms	7 (15.6)	15 (19.2)	22 (17.9)	0.173
	Heat/cold intolerance	9 (20.0)	23 (29.5)	32 (26.6)	0.090
	Hair loss	7 (15.6)	11 (14.1)	18 (14.6)	0.201
	Palpitation	6 (13.3)	11 (14.1)	17 (13.8)	0.213
	Weight loss/gain	15 (33.3)	17 (21.8)	32 (26.0)	0.432
Clinical/cytological diagnosis	Hashimoto’s thyroiditis	43 (95.6)	2 (2.6)	45 (36.6)	0.000
	Multinodular goitre	2 (4.4)	76 (97.4)	78 (63.4)	
Transient hypocalcaemia	Present	32 (71.1)	44 (56.4)	76 (61.8)	0.042
	Absent	13 (28.9)	34 (43.6)	47 (38.2)	
Permanent hypocalcaemia	Present	8 (17.8)	8 (10.3)	16 (13.0)	0.107
	Absent	37 (82.2)	70 (89.7)	107 (87.0)	

HT: Hashimotos thyroiditis. MNG: Multinodular goitre

Table 1 shows that a larger number of females (87.8%) have undergone total thyroidectomy. More than half of the patients belonged to the age group of 30-49 years. Almost all the patients presented with swelling in the neck as the chief symptom, while three had not noticed the palpable swelling. Nearly 80% of the patients did not suffer from pressure symptoms due to the swelling. 26% of the patients experienced heat/cold intolerance and weight gain/loss.

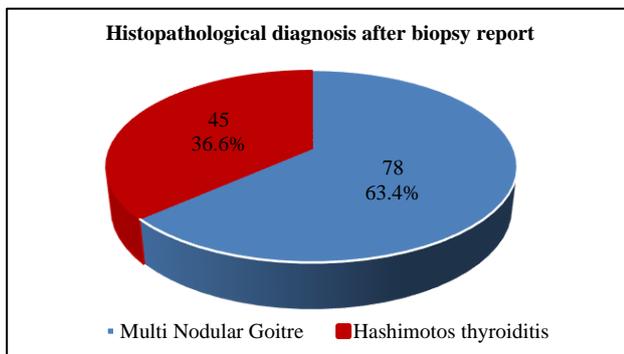


Figure 2: Histopathological diagnosis after biopsy following total thyroidectomy.

Of the 123 total thyroidectomies performed during the period for benign lesions, the biopsy report revealed 45 had Hashimotos disease and 78 had multinodular goitre.

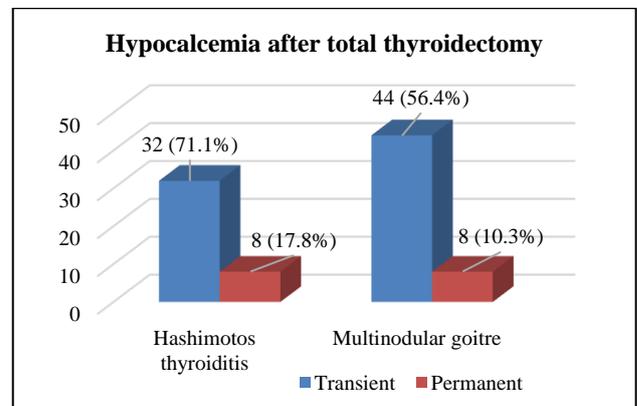


Figure 3: Hypocalcaemia following total thyroidectomy for benign thyroid swellings.

Transient hypocalcaemia: Of the 45 patients with Hashimoto’s thyroiditis who underwent total thyroidectomy, 32 (71.1%) developed transient hypocalcaemia compared to 44 (56.4%) of patients with multinodular goitre (p=0.042).

Permanent hypocalcaemia: There were 8 (17.8%) patients with Hashimoto’s thyroiditis who developed permanent hypocalcaemia compared to 8 (10.3 %) of the 78 patients with multinodular goitre (p=0.107).

After biopsy the histopathological diagnosis showed that 45 (36.6%) were diagnosed to have HT, while 78 (63.4%) had MNG as shown in Figure 2.

During the early post-operative period, the mean serum calcium level in the Hashimoto group was 7.45 (SD 0.77) and in the multinodular goitre group it was 7.62 (SD 0.72). Of the 123 patients who underwent total thyroidectomy, 76 (61.8%) developed transient hypocalcaemia, while 16 (13.0 %) suffered from permanent hypocalcaemia following surgery. The incidence of transient hypocalcaemia following total thyroidectomy was 71.1% in patients with Hashimoto's thyroiditis compared to 56.4% in multinodular goitre ($p=0.042$). The incidence of permanent hypocalcaemia was 17.8% in Hashimoto's thyroiditis while it was 10.3% in multinodular goitre as shown in Figure 3.

DISCUSSION

In this study we found that more than half the patients operated were in the age group 30 to 49 years and over a third were in the age group 50 to 69 years. Most of the patients were females (87.8%). A parallel observation was seen in a similar study where a majority of the patients with benign thyroid lesions were over 40 years of age (52.9%) and of these a majority were females (82.1%).⁵ As most of the participants were females, and a good number were over the age of 50 years, it would have been worthwhile to do the bone mineral density in these patients.

Most of the 123 patients, presented with neck swelling (97.6%), while others had heat or cold intolerance (26.6%), weight gain or loss (26.6%) and/or pressure symptoms (17.9%). Other presenting symptoms were hoarseness of voice, hair loss and palpitations. Viswanathan et al also found that the majority of patients presented with complaints of neck swelling (72.1%) however they also had patients presenting with dysphagia and dyspnoea.⁵

All cases of Hashimoto's thyroiditis were not diagnosed preoperatively as thyroid antibodies were not routinely done for evaluation of thyroid gland enlargement in our institution at that time. When the clinical, sonological and cytological evaluation revealed a symptomatic multinodular thyroid swelling with no conclusive indication of thyroiditis, the decision to perform a total thyroidectomy was made.

The histopathological biopsy report in 78 (63.4%) of the 123 total thyroidectomies done, showed multinodular goitre while HT was the histopathological diagnosis in the remaining 45 (37.1%). Various studies have shown that around 60% of total thyroidectomies were done for multinodular goitre, which is similar to our observation (63.4%) in this study as well.^{5,8} The size of the thyroid swelling varied in all operated specimens. There were no cases with retrosternal extension and none of the patients

required cutting the strap muscle for thyroidectomy. Regarding lymph node status in these thyroidectomies, there was no significant cervical lymphadenopathy and lymph node dissection was not done in any of these patients.

Of the 45 patients with Hashimoto's thyroiditis who underwent total thyroidectomy, 32 (71.1%) had transient hypocalcaemia and 8 (17.8%) developed permanent hypocalcaemia compared to 44 (56.4%) and 8 out of 78 (10.3%) patients with multinodular goitre. Few observational studies had noted up to 50% of transient and 4% permanent hypocalcaemia after thyroidectomy.^{10,11} From our study it was observed that the incidence of post-operative hypocalcaemia was significantly higher in patients who underwent total thyroidectomy for Hashimoto's thyroiditis than for those who underwent the surgery for multinodular goitre ($p=0.04$).

The parathyroid glands control the calcium levels in the blood and the bones. During surgery, due to the difficulty of differentiating between thyroid, fat and parathyroid gland, inadvertent damage may occur to the gland. This can result in hypoparathyroidism leading to hypocalcaemia. Depending on the extent of parathyroid gland damage, hypocalcaemia may be transient, resolving within a few months, or permanent, requiring lifelong oral calcium and vitamin D supplementation.³ The British Association of Endocrine and Thyroid Surgeons reported that 30% of patients after total thyroidectomy have temporary hypocalcaemia and approximately 7% of patients need to take long term calcium and Vitamin D supplements.⁴

In some cases of Hashimoto's thyroiditis, pharmacotherapy and hormone replacement may not suffice to manage the symptoms and surgical therapy is required. Thyroidectomy is indicated in patients suffering from severe, painful goitre or experiencing pressure symptoms resulting from tracheal encroachment, which include dysphasia or dyspnoea. Thomas and Rutledge have attempted to create the following guidelines for thyroid resection:

Dominant mass unresponsive to thyroxine therapy; increase in the size of the mass despite thyroxine therapy; history or physical examination findings suggestive of malignancy and indeterminate findings on cutting needle biopsy.¹²

A small group of patients, with Hashimoto's thyroiditis, present with pain and tenderness and thyroidectomy has been proven to be effective.¹³

Thyroidectomy has become a safe operation with little risk of mortality and long term morbidity. With meticulous operative technique and careful attention to detail, injury to the recurrent laryngeal nerves and superior laryngeal nerves and permanent

hypoparathyroidism can be minimized. This is even true in settings such as re-operations where the risks of injury to these structures are greater from scarring and altered anatomy.¹¹

In our study there were no cases of inadvertent damage to parathyroid glands. All the cases of hypocalcaemia were symptomatic. Only around 50% of patients had carpopedal spasm. None had ECG changes or tetany.

The high incidence of hypocalcaemia, with skilled senior surgeons operating, actually triggered us to consider if there was a higher risk of post-operative hypercalcaemia in patients with Hashimoto's thyroiditis. Though on clinical and sonological examination, there were multiple thyroid nodules the histopathological report diagnosed 45 of the total 123 cases as Hashimoto's thyroiditis, leading us to consider a coexistence of Hashimoto's thyroiditis with multinodular goitre in these patients.

The limitations of this study are the small numbers and the lack of antibody testing for Hashimoto's thyroiditis. The small number of patients of Hashimoto's thyroiditis (45) included in this study may have limited our outcome. More prospective studies need to be done to confirm that there is a real risk in performing total thyroidectomy for Hashimoto's disease.

This study shows the importance of preoperative evaluation of thyroid with thyroid antibodies in diagnosing Hashimoto's thyroiditis especially when there are thyroid nodules. Making a diagnosis based on clinical evaluation and cytological report may lead to missing the thyroiditis component, as the fine needle aspiration cytology (FNAC) may be reported as a colloid nodule. Even with a diagnosis of multinodular goitre there may be a co-existent Hashimoto's thyroiditis, which could be confirmed by doing antibody testing. In any case, it is better to avoid total thyroidectomy in multinodular goitre merely for cosmetic purposes. The significant risk of post-operative hypocalcaemia should be kept in mind and opting for total thyroidectomy for benign lesions of the thyroid must be a last resort only if the symptoms cannot be controlled by pharmacological measures.

CONCLUSION

We would like to conclude that the significant risk of post-operative hypocalcaemia should be kept in mind when opting for total thyroidectomy for benign lesions of the thyroid. The decision to opt for surgery must be made only if significant symptoms persist that are not responding to pharmacological measures. This study throws light on the importance of doing a pre-operative evaluation with antithyroid antibodies to confirm the diagnosis of Hashimoto's thyroiditis especially when there are thyroid nodules.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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