

## Study to Determine the Predictors of Postoperative Hypocalcemia Requiring Augmentation of Routine Calcium Supplementation after Total Thyroidectomy

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### Abstract

**Aim:** The aim of this study was to determine the predictors of postoperative hypocalcemia requiring augmentation of routine calcium supplementation.

**Methods:** The present study collected data of 50 patients who underwent total thyroidectomy with or without central compartment node clearance (CCC) and/or lateral neck dissection (LND) for malignant or benign conditions in the Department of Onco Surgery, Bihar cancer surgical Hospital, Malahi Pakri Chowk, Patna, Bihar, India.

**Results:** Out of these 50 patients, 80% were females. Median age at the time of presentation was 46 years (range 16–80 years). A total of 44 patients (88%) underwent surgery for thyroid cancer, while the remaining 6 (12%) underwent surgery for benign conditions. There were 35 patients (75%) who did not require alteration in routine calcium supplementation, 12 patients (24%) required an increase in oral calcium supplementation, while 3 patients (6%) were escalated to i.v. calcium supplementation for correction of hypocalcemia. There was a significant correlation between the number of congested parathyroid glands at the end of surgery and the requirement of calcium augmentation. Out of 20 patients in the low PTH group, 10 patients (50%) required increase in oral calcium supplementation and 2 patients (10%) required i.v. calcium correction for hypocalcemia. While in the high PTH group (30 patients), only 3 patients (10%) required increase in oral calcium, none requiring i.v. calcium correction. This difference was statistically significant ( $p < 0.001$ ).

**Conclusion:** The risk of developing hypocalcemia and the need for calcium dose augmentation after total thyroidectomy was significantly associated with CCC, parathyroid gland congestion, and serum PTH levels. Identifying parathyroid gland congestion at the end of surgery and measurement of the serum PTH levels are effective strategies in the reduction of morbidity from postoperative hypocalcemia with implications on time and cost.

**Keywords:** Postoperative hypocalcemia, Calcium supplementation, PTH levels, Total thyroidectomy

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## Introduction

Hypocalcemia is one of the major complications of surgical interventions in the central neck (level VI) due to the small size of the parathyroid glands (PGs), their proximity and firm adherence to the thyroid, and the risk of compromising their blood flow during surgery. Despite the expertise of surgeons, postsurgical hypocalcemia remains a prevalent complication in patients undergoing total thyroidectomy and / or central lymph node dissection, causing high postoperative morbidity and compromising the quality of life and increasing costs to the health system. [1]

Thyroid surgery is one of the most frequently performed surgical procedures worldwide. [2] In fact, total thyroidectomy is now widely accepted as the gold standard for the management of thyroid carcinoma and benign bilateral thyroid disease due to suspicion of cancer, symptoms of local compression, and a patient's desire for rapid and definitive treatment. [3] Currently, total thyroidectomy is considered a safe procedure when performed by experienced surgeons. The main postoperative complications are recurrent laryngeal nerve palsy and hypocalcemia. [2,4]

By definition, transient hypocalcemia resolves within 6 months after total thyroidectomy; its reported incidence ranges from 0.3% to 49%. Permanent hypocalcemia persists after 6 months, with an incidence ranging from 0% to 13%. [5] Therefore, hypocalcemia is one of the main outcomes for auditing and patient consent. [6,7] Inpatient admission and close monitoring of postoperative serum calcium level has been proposed to prevent postoperative symptoms related to hypocalcemia. [8] However, this approach has been criticized mainly due to the fact that the lowest concentration of serum calcium is usually not reached until 48–72 hours after thyroidectomy; therefore, it has

major implications for safe early discharge planning. [9]

Transient post-thyroidectomy hypocalcemia is self-limiting, but it could potentially be life-threatening. [10] Hypocalcemia symptoms are uncommon unless serum calcium level is below 8.0 mg/dL (2.0 mmol/L). [11] Symptoms depend on the degree and rapidity of hypocalcemia onset, ranging from mild paresthesia and tingling to more severe cramps, tetany, seizures, laryngospasm, congestive heart failure, and arrhythmias due to prolonged QT intervals. [9,12] Hungry bone syndrome could also occur after total thyroidectomy for Graves' disease as the patient recovers from the disease's thyrotoxic effects on bone metabolism. [13]

To manage postoperative hypocalcemia, most practitioners obtain serial serum calcium measurements and respond appropriately to low levels. [14] Oral supplementation is started with elemental calcium with or without calcitriol for immediate management of postsurgical hypoparathyroidism. [13] For patients whose symptoms persist despite oral replacement therapy, intravenous replacement and closer monitoring are indicated. [9] There are various side effects of hypocalcemia including Chvostek's sign, Trousseau's sign, numbness, and paresthesia that can be worrisome for the patients and may lead to prolonged hospital stays. Long-term hypocalcemia can also lead to skeletal abnormalities. [15,16]

The aim of this study was to determine the predictors of postoperative hypocalcemia requiring augmentation of routine calcium supplementation.

## Materials and Methods

The present study collected data of 50 patients who underwent total thyroidectomy with or without central

compartment node clearance (CCC) and/or lateral neck dissection (LND) for malignant or benign conditions in the Department of Onco Surgery, Bihar cancer surgical Hospital, Malahi Pakri Chowk, Patna, Bihar, India for 1 year.

### Methodology

In order to maintain uniformity of surgical technique, study patients were assigned to the same set of experienced surgeons who performed all the surgeries and evaluated the status of parathyroid glands intraoperatively. All patients received a protocol-mandated dose of calcium (1.5 g/day) and vitamin D3 (0.5 mcg/day) from 1st postoperative day (POD).

### Monitoring of Hypocalcemia

Patients were evaluated for clinical signs and symptoms of hypocalcemia, namely, tingling, numbness, paresthesia, tetany, or Chvostek's sign from POD 1 till the day of discharge. Serum parathyroid hormone (PTH) and calcium levels were measured at 6 AM on POD 1, and serum calcium levels were repeated at POD 2/3, PODs 4-7, PODs 8-14, and PODs 15-21. Hypocalcemia was categorized as clinical or biochemical (serum calcium level < 8.5 mg/dl in the presence of normal serum

albumin), either during the hospital stay or any time after discharge from hospital during postoperative outpatient clinic visits. The need of additional oral or intravenous (i.v.) calcium supplementation over and above the protocol-mandated dose was evaluated as an outcome measure.

### Assessment of Parathyroid Status

Number and color of parathyroid glands identified intraoperatively was recorded. Color of the parathyroid glands was noted at the end of surgery and recorded as congested or non-congested. The need to reimplant unintentionally removed parathyroid gland into the sternocleidomastoid muscle was also documented.

### Statistical Analysis

Descriptive analysis was done for basic epidemiological characteristics. Pearson's chi-square test was used for categorical variables. Logistic regression was used for multivariate analysis. SPSS 17 (SPSS, Inc., Chicago, IL) was used to analyze the data. p value of < 0.05 was considered significant.

### Results

**Table 1: Factors predicting requirement of augmentation in calcium supplementation**

Factors		Augmentation in Calcium Supplementation			P Value
		Not required (n=35)	Oral calcium (n=12)	Intravenous calcium (n=3)	
<b>Gender</b>	Male (10)	6 (60%)	4 (40%)	0	0.610
	Female (40)	30 (75%)	8 (20%)	2 (5%)	
<b>Pathology</b>	Benign (6)	6 (100%)	0	0	0.165
	Malignant (44)	30 (68.18%)	12 (27.28%)	2 (4.54%)	
<b>Lateral Neck Dissection</b>	Not done (30)	22 (73.4%)	7 (23.33%)	1 (3.33%)	0.840
	Unilateral (10)	6 (60%)	4 (40%)	0	
	Bilateral (15)	10 (66.66%)	3 (20%)	2 (13.34%)	
<b>Central Compartment Clearance</b>	Not done (24)	25 (83.34%)	4 (16.66%)	0	0.016
	Unilateral (10)	8 (80%)	2 (20%)	0	
	Bilateral (16)	7 (43.75%)	7 (43.75%)	2 (12.5%)	
<b>Parathyroid Congestion</b>	At least 1 congested (12)	7 (58.33%)	4 (33.33%)	1 (8.34%)	0.025
	None	30 (78.94%)	10 (21.05%)	0	

	congested (38)				
PTH level*	Low (< 11.5pg/ml)[20]	8 (40%)	10 (50%)	2 (10%)	<0.001
	High (> 11.5pg.ml)[30]	27 (90%)	3 (10%)	0	

Out of these 50 patients, 80% were females. Median age at the time of presentation was 46 years (range 16–80 years). A total of 44 patients (88%) underwent surgery for thyroid cancer, while the remaining 6 (12%) underwent surgery for benign conditions. There were 35 patients (75%) who did not require alteration in routine calcium supplementation, 12 patients (24%) required an increase in oral calcium supplementation, while 3 patients (6%) were escalated to i.v. calcium supplementation for correction of hypocalcemia. Augmentation of calcium supplementation was not found to be associated with gender ( $p = 0.610$ ), tumor pathology (benign or malignant) ( $p = 0.165$ ), or lymph node dissection status ( $p = 0.840$ ) on univariate analysis. Bilateral CCC was found to be significantly associated with the need for dose augmentation ( $p = 0.016$ ), with 7 patients needing only oral calcium, while 2 patients needed intravenous correction.

There was a significant correlation between the number of congested parathyroid glands at the end of surgery and the requirement of calcium augmentation. Among patients with at least 1 parathyroid gland congested (12 patients), 4 patients required augmentation of oral calcium and 1 patients required i.v. administration for their symptoms ( $p = 0.025$ ). The patients were divided into two groups (high PTH and low PTH) based on the PTH level of 11.5 pg/ml. Out of 20 patients in the low PTH group, 10 patients (50%) required increase in oral calcium supplementation and 2 patients (10%) required i.v. calcium correction for hypocalcemia. While in the high PTH group (30 patients), only 3 patients (10%)

required increase in oral calcium, none requiring i.v. calcium correction. This difference was statistically significant ( $p < 0.001$ ). On multivariate analysis, only serum PTH showed a significant impact on the need for augmentation of calcium supplementation ( $p = 0.003$ ).

### Discussion

Hypocalcemia secondary to hypoparathyroidism after thyroidectomy is a frequent complication morbidity and mortality. The use of predictive factors allows timely identification of patients at risk and the prevention of complications. Early monitoring of I pth and corrected or ionized serum calcium levels after neck surgery, are the most appropriate tests used to diagnose transitory and permanent hypoparathyroidism. Hypocalcaemia is one of the most common complications of bilateral thyroid surgery. [17-19] The reported incidence of post-thyroidectomy hypocalcaemia ranges widely from 13% to 49%. [19,20]

We have used oral calcium and vitamin D supplementation from POD 1 as routine practice after total thyroidectomy in order to preempt or mitigate the symptoms of hypocalcemia. In spite of this intervention, patients still develop postoperative symptomatic hypocalcemia and require administration of additional calcium, either orally or through the i.v. route. Roh et al. in 2009 published that patients after total thyroidectomy with CCC for papillary carcinoma have a higher incidence of hypocalcemia as compared with patients with total thyroidectomy alone. Routine use of oral calcium and vitamin D supplementation was shown to significantly reduce the incidence of postoperative hypocalcemia.[21] He

showed that in a group of 148 patients who underwent total thyroidectomy with CCC, the incidence of symptomatic and laboratory hypocalcemia was 26% and 44%, respectively, if they did not receive calcium and vitamin D supplementation (n = 50). This incidence reduced to 2% and 8%, respectively, if patients received calcium and vitamin D (n = 50), and to 12.2% and 24.5%, respectively, in patients receiving calcium alone (n = 49). This difference was statistically significant.

The present study reflected similar findings with patients requiring a central compartment clearance in addition to total thyroidectomy having a significantly higher incidence of postoperative hypocalcemia and subsequent escalation of calcium dose compared with patients who had total thyroidectomy alone (p = 0.016). We also found that congestion of the parathyroid gland at the end of total thyroidectomy was significantly associated with a high risk of developing postoperative hypocalcemia and escalation of the prophylactic calcium dose (p = 0.025).

Symptomatic hypocalcaemia exposes patients to physical and mental suffering, and several measures to reduce the risk of postoperative hypocalcaemia have been suggested. These mainly include modifying surgical procedures such as reducing the extent of thyroid surgery, [22] application of alternative surgical instruments, [23,24] and routine or selected calcium and VD supplementation after thyroidectomy. [25] Various predictors of hypocalcaemia following thyroid surgery have been investigated to direct the use of calcium with or without VD supplementation; however, reproducible, reliable, and stable predictors have not yet been established. [25-27] Therefore, routine supplementation of calcium and VD is advocated in many clinical centers. [28-30]

While hypoparathyroidism is a well-known and documented complication of thyroid surgery, it is important to identify a subset of patients with a low risk of developing hypocalcemia, in whom repeated blood sampling may be avoided and early discharge may be contemplated. Inspection and documentation of the parathyroid gland for congestion at the end of total thyroidectomy help in identifying patients with a high risk of developing hypocalcemia. [31]

### Conclusion

The risk of developing hypocalcemia and the need for calcium dose augmentation after total thyroidectomy was significantly associated with CCC, parathyroid gland congestion, and serum PTH levels. Identifying parathyroid gland congestion at the end of surgery and measurement of the serum PTH levels are effective strategies in the reduction of morbidity from postoperative hypocalcemia with implications on time and cost.

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