

# Incidence and Predictors of Post-thyroidectomy Hypocalcemia: A Tertiary Care Experience from North India

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## ABSTRACT

**Background:** Post-thyroidectomy hypocalcemia is a frequent and significant complication that can lead to considerable morbidity. Identifying reliable predictors of this condition is crucial for improving patient outcomes and managing postoperative care effectively.

**Aim:** To determine the incidence and predictors of post-thyroidectomy hypocalcemia in patients treated at a tertiary care hospital in New Delhi.

**Methodology:** A retrospective analysis was conducted on 117 patients who underwent total thyroidectomy between January 2021 and March 2023. Exclusion criteria included patients with prior or concomitant parathyroidectomy, known hyperparathyroidism, and preoperative hypocalcemia. Postoperative serum calcium and intact parathyroid hormone (iPTH) levels were recorded on the first postoperative day (POD1). Patients with biochemical or clinical signs of hypocalcemia were treated accordingly.

**Result:** The incidence of transient hypocalcemia was 46.6%, with 34.16% of patients requiring intravenous calcium infusion. Low iPTH levels and postmenopausal status emerged as significant predictors of hypocalcemia. Patients with low iPTH levels were more likely to require intravenous calcium, and postmenopausal women showed a higher incidence of hypocalcemia compared to premenopausal women (62.5% vs 30%).

**Conclusion:** Low postoperative iPTH levels and postmenopausal status are significant predictors of hypocalcemia in patients undergoing total thyroidectomy. These findings can help in developing targeted management strategies to mitigate the risk of hypocalcemia.

**Recommendation:** Routine measurement of iPTH levels on postoperative day 1 (POD1) should be incorporated into postoperative care protocols to identify patients at risk for hypocalcemia. Special attention should be given to postmenopausal women, and early intervention strategies should be implemented to improve patient outcomes and reduce hospital stay duration. Further prospective studies with larger sample sizes are recommended to validate these findings.

**Keywords:** iPTH, Post-thyroidectomy, Serum calcium, Total thyroidectomy, Transient hypocalcemia.

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## INTRODUCTION

Hypocalcemia is a well-recognized and potentially serious complication following total thyroidectomy, with reported incidence rates ranging from 1.2 to 40% depending on the study and definition used. Post-thyroidectomy hypocalcemia can present with a wide range of symptoms, from subtle biochemical changes that go unnoticed to severe clinical manifestations such as tetany and cardiac arrhythmias. The British Association of Endocrine and Thyroid Surgeons (BAETS) defines post-thyroidectomy hypocalcemia as a corrected calcium level of less than 2.10 mmol/L on the first postoperative day 1 (POD1), highlighting the importance of vigilant monitoring and timely intervention.<sup>1</sup>

Approximately 12.1% of patients may develop permanent hypocalcemia after thyroidectomy, necessitating ongoing treatment to maintain calcium homeostasis at six months. This condition is most commonly attributed to parathyroid gland (PTG) injury, which can arise from several factors, such as PTG devascularization, obstruction of venous drainage, or inadvertent PTG removal.<sup>2,3</sup> Other factors contributing to post-thyroidectomy hypocalcemia include hungry bone syndrome and intraoperative hemodilution.<sup>2,4,5</sup>

Several studies have investigated the incidence and predictors of hypocalcemia following thyroidectomy surgeries. For instance, Sitges-Serra et al. found that approximately 27% of patients undergoing total thyroidectomy experienced transient hypocalcemia, with 3% developing permanent hypocalcemia.<sup>3</sup>

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Pattou et al. identified intraoperative PTG damage, inadvertent parathyroidectomy, and low postoperative intact parathyroid hormone (iPTH) levels as significant predictors of hypocalcemia.<sup>4</sup> The typical complication rates of total thyroidectomy can be from 7.4 to 13.8%.<sup>6</sup> Edafe et al. reported that low postoperative iPTH levels and the extent of thyroid resection were crucial factors in predicting hypocalcemia.<sup>7</sup> Furthermore, Noureldine et al. emphasized the utility of early postoperative iPTH measurements in predicting hypocalcemia, suggesting that patients with low iPTH levels on POD1 are at a higher risk and may benefit from early calcium supplementation.<sup>6</sup>

Despite advancements in surgical techniques and perioperative care, hypocalcemia remains a prevalent issue. The pathophysiology

involves the inadvertent damage or devascularization of the PTGs during thyroidectomy, leading to a temporary or permanent reduction in parathyroid hormone (PTH) secretion. Parathyroid hormone is essential for maintaining calcium balance, as it promotes calcium reabsorption in the kidneys, activates vitamin D, and facilitates the release of calcium from bone. Therefore, a sudden drop in PTH levels post-surgery can precipitate hypocalcemia.

This study seeks to enhance current knowledge by examining the incidence and predictors of post-thyroidectomy hypocalcemia at a tertiary care hospital in New Delhi. By identifying key risk factors such as postoperative iPTH levels and patient demographic characteristics, we aim to develop targeted management strategies to mitigate the risk of hypocalcemia and improve patient outcomes. The findings of this study are expected to inform clinical practitioners, particularly in the context of enhanced recovery after surgery (ERAS) protocols, which prioritize early discharge and minimize hospital stays.

### METHODOLOGY

A retrospective analysis was conducted on 117 patients who underwent total thyroidectomy from January 2021 to March 2023. Patients with prior or concomitant parathyroidectomy, known hyperparathyroidism, and preoperative hypocalcemia were excluded. Clinical assessment for signs and symptoms of hypocalcemia and biochemical analysis of iPTH and serum calcium levels were done. Postoperative calcium levels and iPTH levels on POD1 were recorded. Patients with biochemical or clinical signs of hypocalcemia were treated with oral calcium and vitamin D supplements, and those with severe hypocalcemia received intravenous calcium.

### RESULTS

The incidence of transient hypocalcemia was 46.6%, with 34.16% of patients requiring intravenous calcium infusion. Low iPTH levels were significantly associated with the need for intravenous calcium ( $p < 0.05$ ). Postmenopausal women had a higher incidence of hypocalcemia compared to premenopausal women (62.5% vs 30%,  $p < 0.05$ ) (Table 1, Fig. 1).

Low iPTH values were significantly associated with postoperative IV calcium requirement ( $p < 0.05$ ). There was no linear relationship between iPTH and calcium levels and symptoms. Hence, correlation could not be assessed. Postmenopausal status was found to be a significant predictor of postoperative hypocalcemia, with 62.5% of patients developing hypocalcemia in the postmenopausal group as compared to 30% in the premenopausal group. However, age as well as gender had no significant association with hypocalcemia. Low postoperative

iPTH values and postmenopausal status were independent predictors of hypocalcemia after total thyroidectomy.

### DISCUSSION

The present study investigated the incidence and predictors of post-thyroidectomy hypocalcemia in a tertiary care setting, with a focus on postoperative iPTH levels and patient demographic factors. The incidence of transient hypocalcemia in our cohort was found to be 46.6%, with 34.16% of patients requiring intravenous calcium infusion. These findings provide valuable insights and align with previously published literature, while also highlighting unique aspects of our patient population.

#### Incidence of Hypocalcemia

Our observed incidence of 46.6% is within the range reported in the literature. For instance, Sitges-Serra et al. reported an incidence of transient hypocalcemia at 27%, while Pattou et al. noted an incidence of 40%.<sup>3,4</sup> The variability in incidence rates can be attributed to differences in definitions of hypocalcemia, surgical techniques, and patient populations.

#### Role of Postoperative iPTH

Our study confirmed that low postoperative iPTH levels are a significant predictor of hypocalcemia, consistent with findings from previous research. Noureldine et al. emphasized the predictive value of early postoperative iPTH measurements, reporting that patients with iPTH levels  $< 10$  picogram/milliliter (pg/mL) on

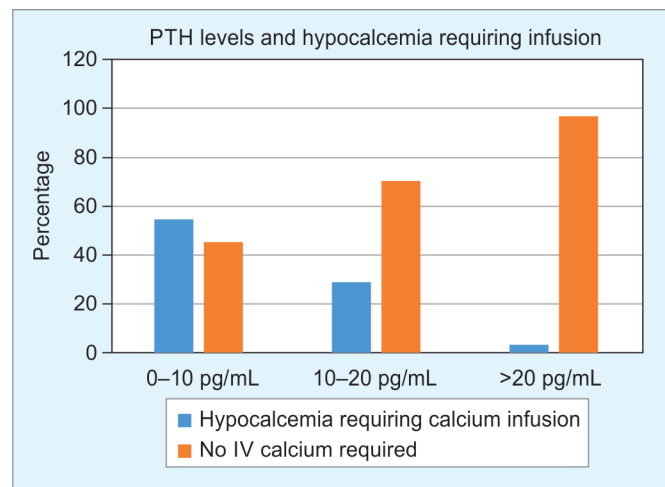


Fig. 1: Co-relation between postoperative iPTH level and hypocalcemia requiring calcium infusion in thyroidectomy patients

Table 1: Co-relation between postoperative iPTH level and hypocalcemia in thyroidectomy patients

iPTH level in postoperative day 1	Total number of patients	Total number of symptomatic patients	Total number of patients with clinical signs of hypocalcemia	Total number of patients with hypocalcemia	Total number of patients with no hypocalcemia	Total number of patients requiring iv infusion of calcium
0-10	44	14 (31.8%)	13 (29.5%)	34 (77.27%)	10 (22.7%)	24 (54.54%)
10-20	17	03 (17.6%)	03 (17.6%)	03 (17.6%)	14 (82.35%)	05 (29.4%)
>20	56	04 (6.8%)	06 (10.3%)	14 (24.13%)	44 (75.8%)	02 (3.4%)
Total	117	21 (17.6%)	22 (18.48%)	51 (42.85%)	68 (57.14%)	31 (26.05%)

POD1 had a higher risk of developing hypocalcemia.<sup>6</sup> Similarly, Edafe et al. found that low iPTH levels were crucial in predicting hypocalcemia, supporting the utility of iPTH as a reliable biomarker for early intervention.<sup>7</sup>

### Demographic Factors

Postmenopausal status was identified as a significant predictor of hypocalcemia in our study. This finding aligns with the study by Edafe et al., which reported higher rates of hypocalcemia in older women.<sup>7</sup> However, the influence of gender and menopausal status has been less frequently highlighted in other studies, suggesting that our findings may offer new insights into patient-specific risk factors.

### IV Calcium Requirement

The regular administration of both calcium and vitamin D supplements following surgery greatly reduces the risk of transient hypocalcemia and acute complications compared to using calcium alone or no supplementation. In instances of hypoparathyroidism, calcitriol is the preferred treatment.<sup>8</sup> In our study, 34.16% of patients required intravenous calcium infusion, indicating a significant burden of severe hypocalcemia. Pattou et al. and Sitges-Serra et al. also reported similar trends, with a subset of patients requiring aggressive calcium management postoperatively.<sup>3,4</sup> This highlights the importance of early identification and treatment of hypocalcemia to prevent severe complications.

Following thyroidectomy, relative parathyroid insufficiency appears to be the leading cause of hypocalcemia, even when postoperative PTH levels fall within the normal range.<sup>9</sup> Promberger's research highlights that intraoperative injury to the PTGs or their blood supply is likely a key factor in the development of permanent hypocalcemia, even when postoperative PTH levels appear normal.<sup>10</sup> Youngwirth et al. reported that postoperative PTH testing is an effective way to identify patients at risk for hypocalcemia following thyroid surgery.<sup>11</sup> Additionally, Cakmakli et al. found that postoperative hypoalbuminemia might indicate a calcitonin leak as the cause of early hypocalcemia onset, while an insufficient parathyroid response may contribute to post-thyroidectomy hypocalcemia.<sup>12</sup>

The study by Lang et al. suggests that measuring rapid parathyroid hormone levels at skin closure (PTH-SC) is both accurate and reliable for predicting clinically significant hypocalcemia, defined as the need for calcium or calcitriol supplementation at discharge. The findings support discharging patients with a PTH-SC level above 1 pmol/L on the same day as their risk of severe hypocalcemia is minimal.<sup>13</sup> Reddy et al. also demonstrated that assessing PTH levels 20 minutes after thyroidectomy effectively predicts clinically relevant hypocalcemia; patients with PTH levels exceeding 9 pmol/L may be safely discharged on the same day with low risk for serious hypocalcemia.<sup>8</sup>

According to Chisthi MM et al., significant hypocalcemia commonly arises within the first 24 hours post-thyroidectomy, primarily due to calcitonin release and hypoalbuminemia. Preserving as many PTGs in situ as possible helps to mitigate and stabilize the drop in calcium levels.<sup>14</sup> Chindavijak showed that measuring intraoperative PTH levels 20 minutes after total thyroidectomy can help predict postoperative hypocalcemia risk, enabling early discharge for stable patients and ensuring appropriate monitoring and supplementation of calcium as needed.<sup>15</sup>

The findings of this study underscore the critical role of postoperative iPTH monitoring in the early identification of patients at risk for hypocalcemia. Incorporating routine iPTH measurements into postoperative care protocols can facilitate timely intervention, reducing the incidence of severe hypocalcemia and associated morbidity. Additionally, recognizing the higher risk in postmenopausal women can help tailor postoperative management strategies to individual patient profiles, improving overall outcomes.

### Limitation of the Study

This study's retrospective design and relatively small sample size are notable limitations. Additionally, we did not assess other potential risk factors such as vitamin D levels and the extent of thyroid disease, which could influence hypocalcemia risk. Future prospective studies with larger cohorts and comprehensive risk factor analysis are warranted to validate and expand upon our findings.

### CONCLUSION

Our study reaffirms the importance of low postoperative iPTH levels and postmenopausal status as significant predictors of post-thyroidectomy hypocalcemia. These findings align with existing literature and highlight the need for targeted management strategies to mitigate the risk of hypocalcemia. Routine iPTH measurement and special attention to high-risk groups such as postmenopausal women should be integral components of postoperative care protocols in thyroidectomy patients.

### Recommendation

Based on our findings, we recommend routine iPTH measurement on the POD1 for all thyroidectomy patients. Enhanced monitoring and early calcium supplementation should be considered for patients with low iPTH levels and postmenopausal women to prevent severe hypocalcemia and improve clinical outcomes. Further research is needed to explore additional risk factors and validate these recommendations in larger, more diverse patient populations.

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