



THE ROLE OF EARLY POSTOPERATIVE PARATHYROID HORMONE IN PREDICTING LONG-TERM HYPOCALCEMIA FOLLOWING TOTAL THYROIDECTOMY: A LONGITUDINAL STUDY

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Abstract

Background: Thyroid diseases are among the most common endocrine disorders worldwide, and India is no exception. Total thyroidectomy has become the primary surgical treatment for many thyroid conditions, including both benign and malignant diseases. This study was therefore designed to prospectively evaluate the incidence of long-term hypocalcemia in patients undergoing total or completion thyroidectomy and to determine the predictive value of PTH and serum calcium levels measured within the first 24 hours post-surgery.

Aim: Role of immediate post operative serum parathyroid hormone (PTH) level to predict long term hypocalcemia in patient undergoing total thyroidectomy

Material and method: A longitudinal study conducted the Dept of E.N.T. RIMS, Imphal. Among 61 patients underwent total thyroidectomy and completion thyroidectomy included in this study for two years, from September 2022 to June 2024. Serum PTH and calcium levels were measured within 24 hours of the surgery. All patients were followed up at 3 months and 6 months postoperatively, with serum calcium levels measured at each visit to assess for recovery or persistence of hypocalcemia.

Results: Our showed pronounced female predominance (96.7%) and a mean age of 44.6 years, with the majority falling within the 41–60-year age group. Preoperative FNAC results were predominantly malignant, with papillary thyroid carcinoma comprising 85.2% of cases. Baseline PTH, serum calcium, and Vitamin D—were within normal reference range. In the immediate postoperative period: hypocalcemia was observed in 96.7% of patients, and 77% developed hypoparathyroidism. At 3 months, 40.9% remained hypocalcemic; however, by 6 months, only 6.55% had persistent hypocalcemia, reflecting substantial restoration of calcium homeostasis.

Conclusion: Overall, thyroidectomy often results in temporary biochemical changes but rarely causes long-term problems. Early postoperative PTH testing is useful for identifying patients at risk and starting treatment promptly, but results should be interpreted cautiously. Ongoing monitoring is important because recovery varies from patient to patient.

Key Word: Total thyroidectomy, parathyroid hormone, hypocalcemia, hypoparathyroidism

INTRODUCTION

Thyroid diseases are one of the most common endocrine disorders globally, and India is no exception, with an estimated 42 million people suffering from these conditions (1). For a wide spectrum of thyroid pathologies, including both benign and malignant diseases, total thyroidectomy has become the mainstay of surgical treatment (2). While this procedure is highly effective, with the risks such as recurrent laryngeal nerve injury, severe bleeding, and postoperative hematoma formation (3). The most frequently encountered complication is hypocalcemia secondary to iatrogenic hypoparathyroidism (4). The primary cause of post-thyroidectomy hypocalcemia is the inadvertent surgical trauma to the parathyroid glands, which can include direct injury, devascularization, or accidental excision causes impaired parathyroid hormone (PTH) secretion (5, 6). The hypocalcemia can be transient, resolving within days or weeks with appropriate supplementation, or it can be permanent if normal calcium homeostasis is not restored within six months. Permanent hypoparathyroidism is a serious long-term complication, reported to occur in 1.3-3% of cases (7, 8). This study was therefore designed to prospectively evaluate the incidence of long-term hypocalcemia in patients undergoing total or completion thyroidectomy and to determine the predictive value of PTH and serum calcium levels measured within the first 24 hours post-surgery.

AIM OF THE STUDY:

Role of immediate post operative serum parathyroid hormone (PTH) level to predict long term hypocalcemia in patient undergoing total thyroidectomy.

MATERIALS AND METHODS

A longitudinal study conducted the Dept of E.N.T. Regional Institute of Medical Sciences, Imphal. The study population included all patients undergoing total thyroidectomy or completion thyroidectomy (for malignancy detected on histopathology after an initial hemithyroidectomy) at our institution. The exclusion criteria were patients with known pre-existing conditions that could alter parathyroid function, such as a parathyroid adenoma, or patients undergoing an intentional primary parathyroidectomy for hyperparathyroidism at the time of thyroidectomy. The required sample size was calculated using the formula $N=4PQ/L^2$. Based on a prior study by Lam et al. (9), the proportion of patients developing postoperative hypocalcemia (P) was estimated to be 30%. With an absolute allowable error (L) set at 8%, the target sample size was 131 patients. However, due to a limited study period and regional disruptions affecting patient access to the hospital, a final sample of 61 patients who met the inclusion criteria and completed the full follow-up was enrolled. The study duration was two years, from September 2022 to June 2024. Serum PTH and calcium levels were measured within 24 hours of the surgery. All patients were followed up at 3 months and 6 months postoperatively, with serum calcium levels measured at each visit to assess for recovery or persistence of hypocalcemia. Ethical approval for the study was obtained from the Research Ethics Board, RIMS, Imphal (Approval No. A/206/REB-Comm(SP)/RIMS/2015/916/254/2022). All participants were provided with a detailed information sheet and gave informed written consent before enrollment in the study. Confidentiality was maintained by assigning a unique code to each participant. All collected data were compiled and analyzed using IBM SPSS Statistics for Windows, Version 26.0 (Armonk, NY: IBM Corp). Descriptive statistics were calculated and presented as frequencies, percentages, means, and standard deviations. The Chi-square test was used to analyze the association between categorical variables, specifically to test the association between immediate postoperative hypoparathyroidism and the development of persistent hypocalcemia at 6 months. A p-value of less than 0.05 was considered to be statistically significant.

Definitions and Variables

- **Hypocalcemia:** Defined as any postoperative serum calcium level below 8.5 mg/dL.
- **Severe/Significant Hypocalcemia:** Defined as a serum calcium level of less than 8.0 mg/dL or the development of any hypocalcemia-related symptoms.

- **Persistent (Long-term) Hypocalcemia:** Defined as hypocalcemia that failed to resolve by the 6-month postoperative follow-up, requiring continued supplementation.
- **Hypoparathyroidism:** Defined as a postoperative PTH level of less than 10 pg/mL, based on our laboratory's reference range of 10-65 pg/mL.

RESULTS

The demographic data revealed a strong female predominance, with 59 females (96.7%) and only 2 males (3.3%). The mean age of the patients was 44.6 ± 12 years, with a range of 20 to 68 years. The largest proportion of patients ($n=32$, 52.5%) fell within the 41-60 years age group.

The preoperative diagnosis, preoperative biochemical parameters were assessed for all patients. The mean preoperative PTH level was 38.8 ± 9.7 pg/mL. The mean preoperative serum calcium level was 9.3 ± 0.4 mg/dL, with a range of 8.2 to 10.2 mg/dL. The mean preoperative Vitamin D level was 38.93 ± 9.43 ng/mL.

Table 1: Distribution of the participants based on the pre-operative diagnosis

Pre-operative diagnosis	Frequency (N=61)	Percentage
Papillary thyroid cancer	52	85.25
Follicular thyroid cancer	6	9.83
Multinodular goitre	1	1.64
Anaplastic carcinoma thyroid	1	1.64
Malignant undifferentiated carcinoma	1	1.64

Table 1: The FNAC Showed, overwhelmingly malignant. Papillary thyroid carcinoma was the most common diagnosis, found in 52 patients (85.2%). Followed by follicular thyroid carcinoma in 6 patients (9.8%). Only one patient each was diagnosed with multinodular goiter, anaplastic carcinoma, and malignant undifferentiated carcinoma.

Figure 1: Histogram depicting preoperative parathyroid hormone levels

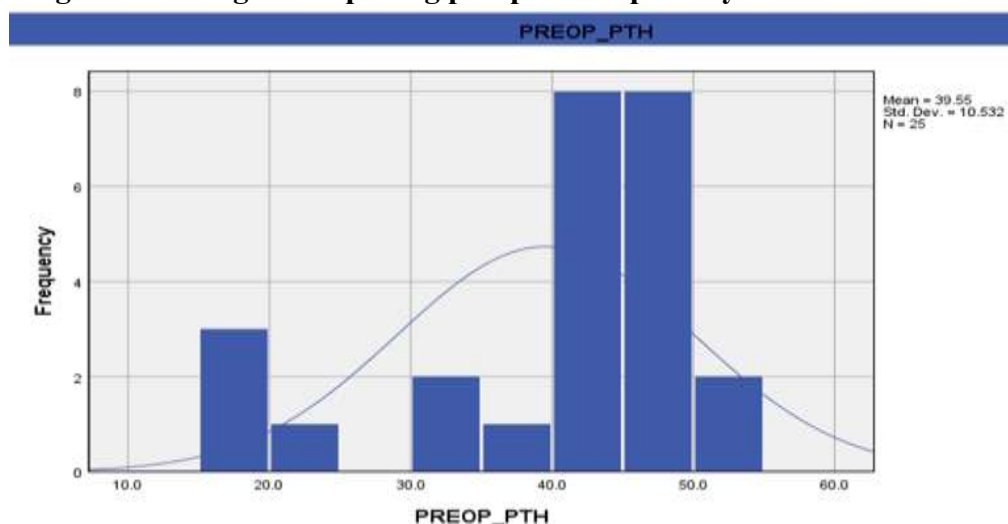


Figure 1: Showed mean pre-operative parathyroid hormone level of 38.8 ± 9.7 with minimum value of 12 pg/ml and maximum value of 54 pg/ml

Figure 2: Histogram Depicting pre-operative serum Calcium levels

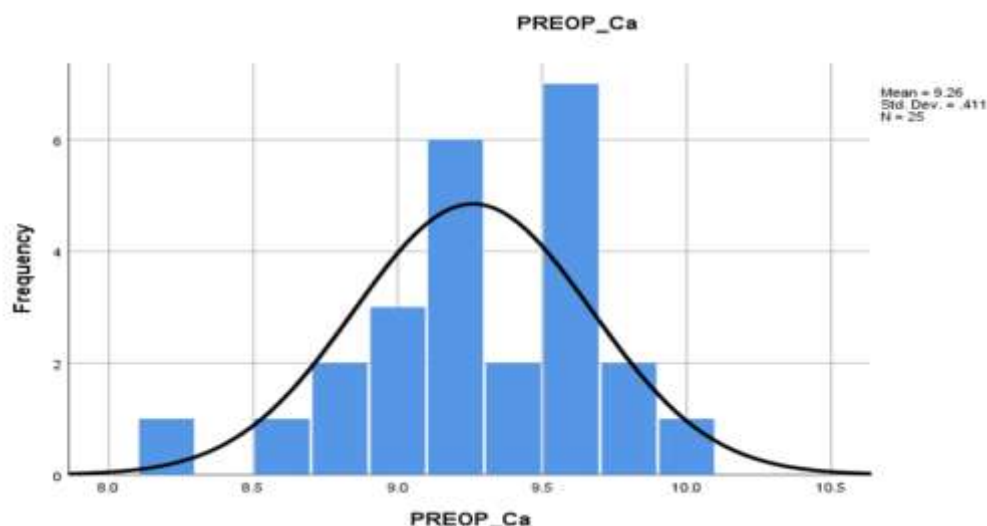


Figure 2: Showed the mean pre operative calcium level of all the patients 9.3 ± 0.4 which was normal. Maximum calcium level was 10.2 mg/dl and minimum being 8.2 mg/ dl.

Figure 3: Histogram depicting pre operative vitamin D Levels

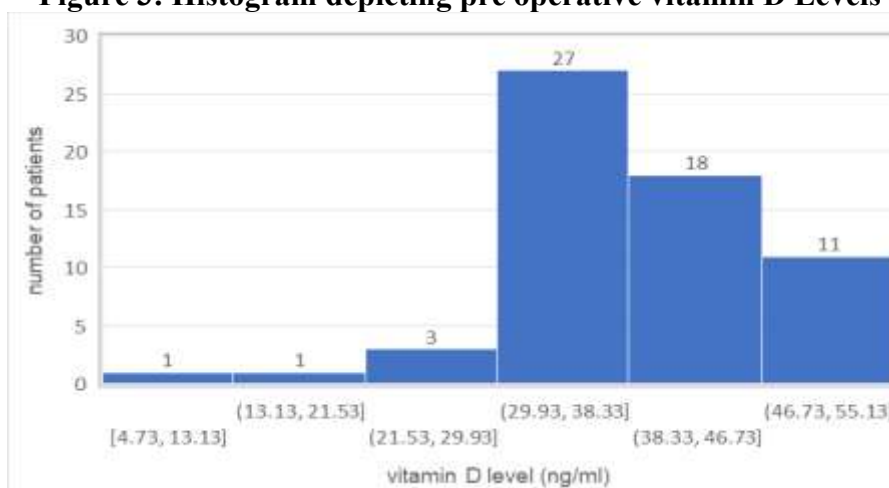


Figure 3: Showed the mean vitamin D level of 38.93 ± 9.43 .

Postoperative Outcomes

Immediate Postoperative Period (within 24 hours): A very high incidence of biochemical disturbances was observed in the immediate postoperative period. Hypocalcemia (serum calcium < 8.5 mg/dL) was detected in 59 out of 61 patients, yielding an incidence of 96.7%. Concurrently, hypoparathyroidism (PTH < 10 pg/mL) was observed in 47 patients, an incidence of 77.05%. A significant overlap was present, with 76.7% of the total cohort experiencing both immediate hypocalcemia and hypoparathyroidism.

Table 3: Percentage of patients with immediate post operative hypoparathyroidism(N=61)

Total patients	61
Patients with post-op hypoparathyroidism	47
Percentage	77.05%

Table 2 shows the percentage of patients with immediate post operative hypoparathyroidism i.e. 77.05% of the patients (n=47).

Table 4: Percentage of participants based on immediate (within 24 hours) post operative calcium level (N=61)

Serum calcium level	Frequency	Percentage
Low	59	96.7
Normal	2	3.3

Table 4 shows that 96.7 percent of the patients had immediate post operative hypocalcemia i.e. 59 out of 61.

Table 5: Distribution of patients based on serum calcium level at 3 months following surgery (N=61)

Serum calcium status	Frequency	Percentage
Low	25	40.9
Normal	36	59.1

Table 5 shows that 40.9 % of the patients have persisting hypocalcemia after 3 months of the surgery i.e. 25 out of 61 patients have hypocalcemia

Table 6: Distribution of patients based on serum calcium level at 6 months following surgery (N=61)

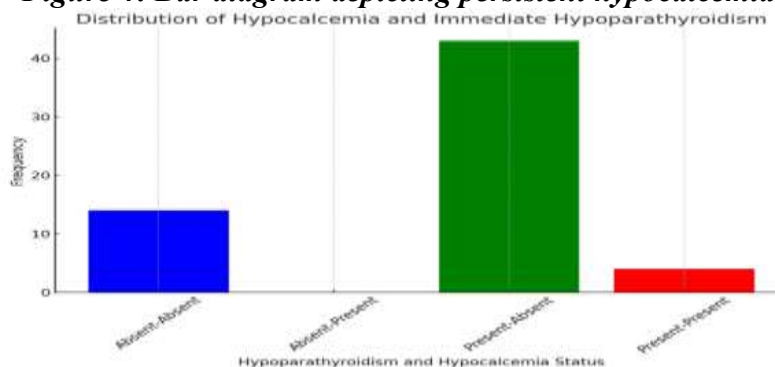
Serum calcium level	Frequency	Percentage
Low	4	6.55
Normal	57	93.44

Table 6 shows 4 patients have persisting hypocalcemia (6.55%) at 6 months after surgery, whereas 57 patients became normocalcemic (93.44%)

Prediction of Long-Term Hypocalcemia

The primary objective was to assess the predictive value of immediate postoperative hypoparathyroidism for long-term hypocalcemia. Of the 47 patients who had immediate hypoparathyroidism, 4 (8.52%) went on to have persistent hypocalcemia at 6 months, while the vast majority, 43 patients (91.48%), recovered. In contrast, among the 14 patients who did *not* have immediate hypoparathyroidism, none (0%) developed persistent hypocalcemia.

Figure 4: Bar diagram depicting persistent hypocalcemia



Although all cases of long-term hypocalcemia arose from the group with initial hypoparathyroidism, the Chi-square analysis did not find a statistically significant association between the presence of immediate hypoparathyroidism and the outcome of persistent hypocalcemia at 6 months ($p=0.26$).

Table 7: Association between immediate hypoparathyroidism and persistent hypocalcemia

Immediate hypoparathyroidism	Hypocalcemia at 6 months n (%)		P value
	Absent	Present	
Absent (n=14)	14 (100)	0 (0)	0.26
Present (n=47)	43(91.48)	4 (8.52)	

Table 7: Showed that the observed frequencies of patients with and without immediate postoperative hypoparathyroidism, cross tabulated with those who did and did not have hypocalcemia at 6 months. None among the 14 patients without hypoparathyroidism had hypocalcemia at 6 months, 43 out of 47 patients who had immediate hypoparathyroidism did not have hypocalcemia at 6 months while 4 had persistent hypocalcemia. The P value of 0.26 (>0.05) suggesting no statistically significant association between immediate hypoparathyroidism and persistent hypocalcemia at 6 months.

DISCUSSION

This study provides a prospective analysis of the incidence and predictors of long-term hypocalcemia following total thyroidectomy in a tertiary care setting. Our findings confirm that while immediate postoperative biochemical disturbances are exceedingly common, the risk of permanent complications is low, and that the predictive utility of early PTH measurement for long-term outcomes may be limited. The demographic profile of our cohort, characterized by a strong female predominance and a mean age in the mid-40s, is highly consistent with the established epidemiology of thyroid cancer, particularly papillary thyroid carcinoma, as reported in numerous other studies (9, 10). The high rate of malignancy (over 95%) in our study population underscores the referral patterns to a tertiary center and inherently places the cohort at a higher risk for postoperative complications due to the frequent necessity of more extensive surgical dissection. A striking finding from our study is the near-universal incidence of immediate postoperative hypocalcemia (96.7%) and the very high rate of immediate hypoparathyroidism (77.05%). This incidence is higher than that reported in some series, such as the 30% rate of hypocalcemia noted by Lam and Kerr (9). However, it is more comparable to studies involving high-risk populations. For instance, Saad M. Alqahtani et al. also reported a high rate of temporary hypocalcemia, especially after total thyroidectomy (11). This high rate in our study is likely multifactorial. The prevalence of thyroid cancer requiring more extensive surgery, including central neck dissection in some cases, is a major contributing factor. Furthermore, baseline factors such as lower-normal preoperative calcium levels and potential subclinical Vitamin D deficiency, which can be common in the female population of the region, may predispose patients to a more pronounced postoperative drop in serum calcium. The central question of our research was whether this early biochemical insult could predict long-term parathyroid function. Our results present a nuanced picture. On one hand, a preserved PTH level in the first 24 hours was an excellent negative predictor: none of the 14 patients with normal early PTH developed long-term hypocalcemia. This aligns with the consensus that a normal postoperative PTH is highly reassuring (12,13). On the other hand, the positive predictive value of a low PTH level was poor. The vast majority (91.48%) of patients who experienced an initial drop in PTH recovered normal calcium homeostasis by the 6-month mark. This led to our primary finding: the association between immediate hypoparathyroidism and persistent hypocalcemia was not statistically significant ($p=0.26$). This lack of a strong statistical link suggests that an early PTH measurement, while an excellent indicator of acute parathyroid gland insult, cannot reliably differentiate between transient dysfunction (often termed parathyroid "stunning" due to edema or temporary ischemia) and permanent, irreversible damage. This finding is

supported by studies like that of Mercante et al., who also found PTH to have low sensitivity as a predictor of transient hypocalcemia (14). It contrasts, however, with other reports where early PTH was found to be a highly reliable predictor of both transient and permanent hypoparathyroidism (15,16,17). This ongoing debate in the literature suggests that the predictive accuracy of PTH may be influenced by the specific timing of the assay, the chosen threshold, the patient population, and surgical technique. The robust recovery of function seen in our patients, with the hypocalcemia rate dropping from 40.9% at 3 months to 6.55% at 6 months, highlights the remarkable capacity of the parathyroid glands to recover from surgical trauma.

LIMITATIONS OF THE STUDY

The final sample size of 61 was smaller than the calculated target, which may have limited the statistical power to detect a true association, potentially leading to a Type II error. The study was also conducted at a single institution with a multi-surgeon series, which could introduce variability in surgical technique and outcomes.

CONCLUSION

Postoperative hypocalcemia is common after total thyroidectomy but is usually temporary. In our study, only a small proportion of patients (6.55%) had persistent hypocalcemia at six months, indicating good overall recovery of parathyroid function. Although a low immediate postoperative PTH level helped identify patients at risk for early hypocalcemia, it did not reliably predict long-term outcomes. More extensive neck dissections were associated with more severe cases. Thus, while thyroidectomy carries low long-term morbidity, clinicians should expect a high rate of transient hypocalcemia. Early PTH measurement is useful for guiding short-term management, but continued monitoring is essential as recovery varies between patients.

REFERENCES

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. *Indian J Endocrinol Metab*. 2011 Jul;15(2):78-81.
2. Harris AS, Prades E, Tkachuk O, Zeitoun H. Better consenting for thyroidectomy: who has an increased risk of postoperative hypocalcemia? *Eur Arch Otorhinolaryngol*. 2016;273:4437-43.
3. Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. *Arch Otolaryngol*. 2002;128:389-92.
4. Sands NB, Payne RJ, Côté V, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. *Otolaryngol Head Neck Surg*. 2011;145(4):561-4.
5. Glinioer D, Andry G, Chantrain G, Samil N. Clinical aspects of early and late hypocalcaemia after thyroid surgery. *Eur J Surg Oncol*. 2000 Sep;26(6):571-7.
6. McHenry CR, Speroff T, Wentworth D, Murphy T. Risk factors for postthyroidectomy hypocalcemia. *Surgery*. 1994 Oct;116(4):641-7.
7. Chadwick DR. Hypocalcaemia and permanent hypoparathyroidism after total/bilateral thyroidectomy in the BAETS Registry. *Gland Surg*. 2017;6:S69-S74.
8. Karadeniz E, Akcay MN. Risk factors of incidental parathyroidectomy and its relationship with hypocalcemia after Thyroidectomy: A retrospective study. *Cureus*. 2019 Oct 16;11(10):e5920.
9. Lam A, Kerr PD. Parathyroid hormone: an early predictor of post thyroidectomy hypocalcemia. *Laryngoscope*. 2003 Dec;113(12):2196-200.
10. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. *Arch Surg*. 2008 Feb;143(2):132-7.
11. Alqahtani SM, Alatawi AS, Alalawi YS. Post-Thyroidectomy Hypocalcemia: A Single-Center Experience. *Cureus*. 2021 Nov 29;13(11):e20006. doi: 10.7759/cureus.20006. PMID: 34987897; PMCID: PMC8716130.
12. Lindblom P, Westerdahl J, Bergenfelz A. Low parathyroid hormone levels after thyroid surgery: a feasible predictor of hypocalcemia. *Surgery*. 2002;131:515-20.

13. Vescan A, Witterick I, Freeman J. Parathyroid hormone as a predictor of hypocalcaemia after thyroidectomy. *Laryngoscope*. 2005;115(12):2105-2108.
14. Mercante G, Anelli A, Giannarelli D, Giordano D, Sinopoli I, Ferreli F et al. Cost-effectiveness in transient hypocalcemia post-thyroidectomy. *Head Neck*. 2019 Nov;41(11):3940-7.
15. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. *Arch Surg*. 2008;143(2):132-138.
16. Quiros RM, Pesce CE, Wilhelm SM, Djuricin G, Prinz RA. Intraoperative parathyroid hormone levels in thyroid surgery are predictive of postoperative hypoparathyroidism and need for vitamin D supplementation. *Am J Surg*. 2005;189(3):306-309.
17. Seo ST, Chang JW, Jin J, Lim YC, Rha KS, Koo BS. Transient and permanent hypocalcemia after total thyroidectomy: Early predictive factors and long-term follow-up results. *Surgery*. 2015;158(6):1492-1499.