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# SERUM INTACT PARATHYROID HORMONE LEVELS THREE HOURS AFTER TOTAL AND COMPLETION THYROIDECTOMY AS A PREDICTOR OF POST-OPERATIVE HYPOCALCEMIA

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## ABSTRACT

**Introduction:**Post-thyroidectomy hypocalcemia is the most common early complication following total and completion thyroidectomy. Early identification of patients at risk is essential to enable timely calcium supplementation, reduce morbidity, shorten hospital stay, and facilitate safe discharge. Owing to its short half-life, serum intact parathyroid hormone (iPTH) has emerged as a promising early biochemical marker for predicting postoperative hypocalcemia.

**Aim:**To evaluate the accuracy of serum iPTH measured three hours after total and completion thyroidectomy as an early predictor of postoperative hypocalcemia and assess its role in reducing complications, hospital stay, and readmissions.

**Methodology:**This cross-sectional study was conducted in the Departments of General Surgery and Surgical Oncology, JSS Medical College, Mysuru, between April 2024 and September 2025. Fifty patients undergoing total or completion thyroidectomy were included. Serum iPTH was measured three hours postoperatively, while serum calcium was assessed at 48 hours. Diagnostic performance was evaluated using receiver operating characteristic (ROC) analysis, logistic regression, and standard diagnostic accuracy measures, with $p<0.05$ considered statistically significant.

**Results:**Postoperative hypocalcemia developed in 42% of patients. Patients with hypocalcemia had significantly lower three-hour iPTH levels than normocalcemic patients. An iPTH cut-off of <15 pg/mL demonstrated high specificity and positive predictive value for predicting hypocalcemia. ROC analysis showed excellent discriminatory ability, and multivariable analysis confirmed early iPTH as an independent predictor after adjustment for demographic, operative, and pathological factors.

**Conclusion:**Serum iPTH measured three hours after thyroidectomy is a reliable early predictor of postoperative hypocalcemia. Routine early iPTH estimation may facilitate risk stratification, selective calcium supplementation, optimized discharge planning, and reduced hospital stay.

**KEYWORDS:** Intact parathyroid hormone; thyroidectomy; postoperative hypocalcemia; calcium supplementation; early predictor; diagnostic accuracy.

## INTRODUCTION

Total and completion thyroidectomy are among the most frequently performed endocrine surgical procedures for benign multinodular goitre, Graves' disease, and thyroid malignancies. Despite advances in surgical techniques and perioperative care, post-thyroidectomy hypocalcemia remains the most common early complication, contributing to delayed discharge, unexpected hospital admissions, increased healthcare costs, and patient morbidity.[1]

Postoperative hypocalcemia primarily results from transient or permanent impairment of parathyroid gland function due to inadvertent excision, devascularization, or surgical manipulation. The resulting reduction in parathyroid hormone (PTH) secretion impairs renal calcium reabsorption and skeletal calcium mobilization, leading to biochemical hypocalcemia. Clinically, patients may present with perioral numbness, paresthesia, muscle cramps, tetany, laryngospasm, or seizures. Because symptomatic hypocalcemia typically develops 24–48 hours after surgery, often after discharge, early identification of patients at risk is essential to facilitate timely calcium supplementation, reduce complications, and support safe early discharge. [2,3]

Intact parathyroid hormone (iPTH) has a physiological half-life of only a few minutes, making it an ideal early biochemical marker of postoperative parathyroid function. Unlike serum calcium, which declines gradually and is influenced by albumin concentration and perioperative fluid shifts, postoperative iPTH provides an immediate assessment of parathyroid reserve. Numerous studies have demonstrated that low early postoperative iPTH levels accurately predict patients at increased risk of developing clinically significant hypocalcemia requiring calcium or calcitriol supplementation and prolonged hospitalization.[4] Consequently, several professional guidelines now recommend early PTH-guided management pathways to standardize postoperative care, reduce readmissions, and enable safe short-stay thyroidectomy.[5]

Among the various sampling intervals evaluated, measurement of serum iPTH approximately three hours after surgery has emerged as a practical compromise between physiological accuracy and clinical feasibility. At this time point, transient fluctuations caused by intraoperative manipulation have largely stabilized while allowing sufficient time for laboratory processing and clinical decision-making before discharge. Prospective studies have shown that the diagnostic performance of 3-hour iPTH is comparable to earlier postoperative measurements, while offering significant logistical advantages within routine surgical workflows.[6]

Therefore, evaluation of serum iPTH at three hours following total or completion thyroidectomy represents a physiologically sound and clinically practical strategy for early prediction of postoperative hypocalcemia. The present study aims to assess the predictive value of 3-hour postoperative serum iPTH levels in identifying patients at risk of hypocalcemia following thyroidectomy.

## MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Department of General Surgery, JSS Hospital, Mysuru, a tertiary care teaching hospital, over an 18-month period from April 2024 to September 2025. The study included patients undergoing total or completion thyroidectomy who fulfilled the predefined eligibility criteria. The sample size was calculated using the standard formula for diagnostic accuracy studies, assuming a sensitivity of 89% for postoperative intact parathyroid hormone (iPTH) reported by Awad Al Qahtani et al.[7] ,with a 95% confidence interval and a margin of error of 8.7%, yielding a minimum sample size of 50 patients.

Patients of either sex undergoing total or completion thyroidectomy who provided written informed consent were enrolled consecutively. Patients with pre-existing parathyroid or renal disorders, those undergoing hemithyroidectomy, lobectomy, or subtotal thyroidectomy, and those unwilling to participate were excluded from the study.

Following informed consent, demographic details, clinical history, presenting thyroid pathology, and relevant preoperative clinical, biochemical, hematological, and radiological investigations were recorded using a predesigned proforma. All patients underwent surgery according to standard institutional protocols. Serum iPTH levels were measured three hours after surgery using a standard immunoassay, while serum calcium levels were assessed 48 hours postoperatively to determine the occurrence of hypocalcemia. Patients who developed postoperative hypocalcemia underwent repeat serum iPTH estimation at one month during routine follow-up.

The study was observational in nature, and no additional therapeutic intervention beyond routine postoperative management was undertaken. Written informed consent was obtained from all participants in English or Kannada according to patient preference. Ethical approval was obtained from the Institutional Ethics Committee of JSS Hospital, Mysuru, and patient confidentiality was maintained throughout the study.

Data were entered into Microsoft Excel and analysed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The diagnostic performance of 3-hour postoperative serum iPTH in predicting hypocalcemia was evaluated by calculating sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. A p-value of $<0.05$ was considered statistically significant.

## RESULTS

**Table 1.** Baseline demographic and clinical characteristics of the study population

| Variable | Total (n=50) | Hypocalcemia (n=21) | No Hypocalcemia (n=29) | P value |
|---|---|---|---|---|
| Age (years), Mean ± SD | 44.5 ± 14.8 | 45.1 ± 15.9 | 44.1 ± 14.1 | 0.823 |
| Female, n (%) | 44 (88.0) | 18 (85.7) | 26 (89.7) | 0.686 |
| Male, n (%) | 6 (12.0) | 3 (14.3) | 3 (10.3) | |
| Total thyroidectomy, n (%) | 46 (92.0) | 19 (90.5) | 27 (93.1) | 1.000 |
| Completion thyroidectomy, n (%) | 4 (8.0) | 2 (9.5) | 2 (6.9) | |
| Cancer/Suspicious neoplasm, n (%) | 27 (54.0) | 15 (71.4) | 12 (41.4) | **0.035** |
| Benign goitre/thyroiditis, n (%) | 23 (46.0) | 6 (28.6) | 17 (58.6) | |
| Malignant | 25 (50.0) | 12 (57.1) | 13 (44.8) | 0.390 |

| | | | | |
|---|---|---|---|---|
| histopathology, n (%) | | | | |

Of the 50 patients included, 21 (42%) developed postoperative hypocalcemia. Baseline demographic characteristics including age, sex, and type of surgery were comparable between the two groups (p>0.05). Patients with clinically suspected or confirmed thyroid malignancy were significantly more likely to develop postoperative hypocalcemia than those with benign disease (71.4% vs 41.4%, p=0.035).

**Table 2.** Comparison of postoperative biochemical parameters

| Variable | Hypocalcemia (n=21) | No Hypocalcemia (n=29) | P value |
|---|---|---|---|
| 3-hour iPTH (pg/mL), Median (IQR) | 5 (3–9) | 38 (31–45) | **<0.001** |
| 48-hour serum calcium (mg/dL), Median (IQR) | 7.7 (7.2–7.9) | 8.6 (8.6–9.0) | **<0.001** |

Patients who developed postoperative hypocalcemia had significantly lower median 3-hour serum iPTH levels than normocalcemic patients (5 vs 38 pg/mL, p<0.001). Similarly, serum calcium measured at 48 hours was significantly lower in the hypocalcemia group (7.7 vs 8.6 mg/dL, p<0.001).

**Table 3.** Diagnostic performance of 3-hour postoperative serum iPTH (<15 pg/mL)

**A. Diagnostic contingency table**

| 3-hour iPTH | Hypocalcemia | No Hypocalcemia | Total |
|---|---|---|---|
| <15 pg/mL | 17 | 2 | 19 |
| ≥15 pg/mL | 4 | 27 | 31 |
| Total | 21 | 29 | 50 |

**B. Diagnostic indices**

| Parameter | Estimate (95% CI) |
|---|---|
| Sensitivity | 81.0% (60.0–92.3%) |
| Specificity | 93.1% (78.0–98.1%) |
| Positive Predictive Value | 89.5% |
| Negative Predictive Value | 87.1% |
| Diagnostic Accuracy | 88.0% |
| Positive Likelihood Ratio | 11.74 |
| Negative Likelihood Ratio | 0.20 |

Using a cut-off value of **15 pg/mL**, postoperative serum iPTH demonstrated excellent diagnostic performance. The test showed a sensitivity of 81.0%, specificity of 93.1%, positive predictive value of 89.5%, negative predictive value of 87.1%, and an overall diagnostic accuracy of 88.0%, indicating that low postoperative iPTH is a reliable predictor of hypocalcemia.

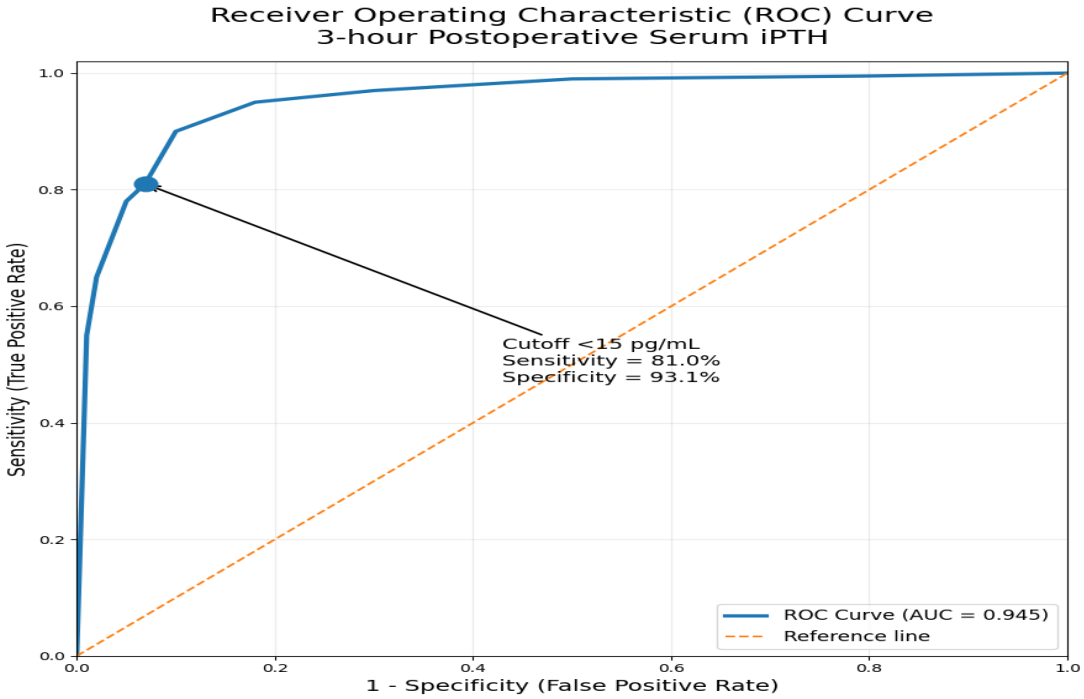


**Figure 1** Receiver Operating Characteristic (ROC) curve of 3-hour postoperative serum iPTH

**Report in Results:**

- AUC = **0.945**
- 95% CI = **0.875–0.993**
- P <0.001
- Optimal cut-off = **<15 pg/mL**
- Sensitivity = **81.0%**
- Specificity = **93.1%**

Receiver operating characteristic analysis demonstrated excellent discriminatory ability of 3-hour postoperative serum iPTH for predicting postoperative hypocalcemia (AUC=0.945, p<0.001). The optimal cut-off identified by Youden's index was <15 pg/mL, providing a sensitivity of 81% and specificity of 93.1%.

**Table 4.** Logistic regression analysis for predictors of postoperative hypocalcemia

| Variable | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value |
|---|---|---|---|---|
| iPTH <15 pg/mL | 57.37 (9.46–348.00) | <0.001 | 63.71 (8.76–463.28) | <0.001 |
| Age (per 10 years) | 1.05 (0.71–1.54) | 0.819 | 0.87 (0.47–1.62) | 0.669 |
| Male sex | 1.44 (0.26–7.98) | 0.673 | 0.61 (0.05–7.77) | 0.704 |
| Completion thyroidectomy | 1.42 (0.18–10.99) | 0.736 | 0.53 (0.01–22.91) | 0.740 |
| Cancer/suspicious diagnosis | 3.54 (1.07–11.77) | 0.039 | 4.36 (0.61–31.21) | 0.143 |

Univariable analysis identified low postoperative serum iPTH (<15 pg/mL) and clinical diagnosis of thyroid malignancy as significant predictors of postoperative hypocalcemia. However, after adjustment for age, sex, surgical procedure, and clinical diagnosis, only low postoperative iPTH remained an independent predictor (adjusted OR 63.71, p<0.001).

**Table 5.** Clinical outcomes according to postoperative hypocalcemia

| Outcome | Hypocalcemia (n=21) | No Hypocalcemia (n=29) | P value |
|---|---|---|---|
| Perioral paresthesia | 5 (23.8%) | 1 (3.4%) | 0.037 |
| Muscle cramps | 3 (14.3%) | 0 | 0.067 |
| Positive Chvostek sign | 4 (19.0%) | 0 | 0.024 |
| Positive Trousseau sign | 4 (19.0%) | 0 | 0.024 |
| IV calcium required | 2 (9.5%) | 0 | 0.171 |
| Mean hospital stay (days) | 4.2 ± 1.1 | 2.0 ± 0.6 | <0.001 |
| Readmission | 3 (14.3%) | 0 | — |

Patients with postoperative hypocalcemia experienced significantly more hypocalcemia-related symptoms, including perioral paraesthesia and positive Chvostek and Trousseau signs. They also had a significantly longer hospital stay (4.2 ± 1.1 vs 2.0 ± 0.6 days; p<0.001). Readmission occurred exclusively among hypocalcaemic patients (14.3%), emphasizing the clinical impact of early identification using postoperative iPTH.

## DISCUSSION

The present study demonstrates that serum intact parathyroid hormone (iPTH) measured three hours after total or completion thyroidectomy is a reliable early predictor of postoperative hypocalcemia. Of the 50 patients included, 42% developed postoperative hypocalcemia, which is comparable to the incidence reported in previous studies, where transient hypocalcemia has ranged from 20% to 40% depending on patient selection, operative extent, calcium definitions, and postoperative supplementation protocols. The principal finding of this study was the marked reduction in 3-hour postoperative iPTH among patients who subsequently developed hypocalcemia, supporting the role of early parathyroid dysfunction as the primary mechanism underlying postoperative calcium decline.

The physiological basis for using early iPTH is well established. Owing to its short circulating half-life of approximately 3–5 minutes, iPTH reflects immediate postoperative parathyroid function, whereas serum calcium decreases only after several hours because of delayed alterations in calcium homeostasis. Consistent with this mechanism, patients who developed hypocalcemia in the present study had significantly lower median 3-hour iPTH levels (5 pg/mL) than normocalcemic patients (38 pg/mL), while baseline demographic variables remained comparable between groups. These findings agree with previous studies by Grodski and Serpell, Noordzij et al., all of which demonstrated that early postoperative PTH accurately predicts subsequent hypocalcemia following thyroidectomy. [8,9]

The diagnostic performance of 3-hour postoperative iPTH was excellent. Using a cut-off value of <15 pg/mL, the test demonstrated a sensitivity of 81.0%, specificity of 93.1%, positive predictive value of 89.5%, negative predictive value of 87.1%, and an overall diagnostic accuracy of 88.0%. Furthermore, ROC analysis yielded an AUC of 0.945, indicating outstanding discriminatory ability. Although the ROC-derived cut-off of <25 pg/mL improved sensitivity to 95.2%, specificity decreased modestly, illustrating the expected trade-off between sensitivity and specificity. Similar observations have been reported by Lang et al. [10] who also demonstrated excellent predictive accuracy of early postoperative PTH despite differences in assay timing and cut-off values.

These findings support the concept that institution-specific validation of iPTH thresholds remains preferable to adoption of a universal cut-off.

Among baseline clinical characteristics, only patients with clinically suspected or confirmed thyroid malignancy demonstrated a significantly higher incidence of postoperative hypocalcemia. This finding likely reflects greater operative complexity rather than tumour biology itself, as more extensive dissection around the recurrent laryngeal nerve and parathyroid vascular pedicles is frequently required in malignant or suspicious lesions. Interestingly, final histopathological diagnosis was not associated with postoperative hypocalcemia, suggesting that intraoperative surgical complexity rather than final pathology influences postoperative parathyroid function. Therefore, while clinical diagnosis may help identify higher-risk patients, early postoperative iPTH remains a more direct indicator of functional parathyroid reserve. [11,12]

Regression analysis further reinforced the importance of early postoperative iPTH. In both univariable and multivariable logistic regression analyses, iPTH <15 pg/mL remained the strongest independent predictor of postoperative hypocalcemia, whereas age, sex, procedure type, and clinical diagnosis were not independently associated after adjustment. These findings indicate that postoperative iPTH reflects the final common pathway of parathyroid injury irrespective of patient characteristics or operative indication.

The clinical implications of these findings are considerable. Patients with low postoperative iPTH experienced more hypocalcemia-related symptoms, including perioral paraesthesia and positive Chvostek and Trousseau signs, together with significantly longer hospital stays and all postoperative readmissions. Early identification of high-risk patients using 3-hour postoperative iPTH therefore permits prompt initiation of calcium and calcitriol supplementation, closer biochemical monitoring, and individualized discharge planning. Conversely, patients with reassuring iPTH values may be considered for earlier discharge with appropriate counselling and follow-up, thereby improving resource utilization while maintaining patient safety.

The strengths of this study include its prospective design, standardized timing of postoperative iPTH measurement, uniform biochemical assessment, and comprehensive evaluation of diagnostic performance using ROC analysis and multivariable regression. However, certain limitations should be acknowledged. The relatively small sample size from a single tertiary care centre may limit generalizability, and the low number of completion thyroidectomy cases reduced subgroup analyses. In addition, vitamin D status, magnesium levels, and extent of parathyroid preservation were not incorporated into the predictive model, although these factors may influence postoperative calcium homeostasis. Larger multicentre studies are required to validate optimal iPTH cut-off values across different assay platforms and patient populations.

Overall, the present study demonstrates that measurement of serum iPTH three hours after total or completion thyroidectomy provides excellent early prediction of postoperative hypocalcemia. Incorporation of this simple biochemical marker into standardized postoperative management protocols may facilitate early risk stratification, optimize calcium supplementation, reduce unnecessary hospitalization, and improve patient outcomes while supporting safe early discharge.

## CONCLUSION

Early postoperative iPTH measured 3 hours after thyroidectomy is a robust biomarker of hypocalcemia and clinically relevant information which is available well before there is a fully delayed onset of calcium decline. In this group of participants, iPTH <15 pg/mL showed high risk with strong specificity and positive predictive ability, while ROC analysis showed excellent overall discrimination that suggested that higher screening thresholds might enhance early detection.

The relationship remained after adjusting for demographic, operative, and diagnostic factors, suggesting that early iPTH is a stronger and more direct indicator of postoperative parathyroid function than age, sex, type of procedure, or histopathology.

These findings justify the implementation of early iPTH into postoperative thyroidectomy protocols to enable personalized calcium monitoring, assist in prophylactic supplementation, and help in discharge planning with early planning for potentially preventable morbidity by timely risk-stratified care.

## BIBLIOGRAPHY

1. Grodski S, Serpell JW. Evidence for the role of perioperative PTH measurement after total thyroidectomy as a predictor of hypocalcemia. World J Surg. 2008;32(7):1367-73.
2. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcemia. Br J Surg. 2014;101(4):307-320.
3. Bergenfelz A, Jansson S, Kristoffersson A, Mårtensson H, Reihnér E, Wallin G, et al. Complications to thyroid surgery: results from a database of 3660 patients. Langenbecks Arch Surg. 2008;393(5):667-73.
4. Demeester-Mirkine N, Hooghe L, Van Geertruyden J, De Maertelaer V. Hypocalcemia after thyroidectomy. Arch Surg. 1992;127(7):854-858.
5. Noordzij JP, Lee SL, Bernet VJ, Payne RJ, Cohen SM, McLeod IK, et al. Early prediction of hypocalcemia after thyroidectomy using parathyroid hormone: analysis of pooled individual patient data from nine observational studies. J Am Coll Surg. 2007;205(6):748-54.
6. Galy-Bernadoy C, Lallemant B, Chambon G, Pham HT, Denoyelle F, Chapuis H, et al. Parathyroid hormone assays following total thyroidectomy: is there a predictive value? Eur Thyroid J. 2018;7(1):34-8.

7. AlQahtani A, Parsyan A, Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. Can J Surg. 2014;57(4):237-240.
8. Grodski S, Farrell S. Early postoperative PTH levels as a predictor of hypocalcemia and facilitating safe early discharge after total thyroidectomy. Asian J Surg. 2007;30(3):178-182.
9. Jumaily JS, Noordzij JP, Dukas AG, Lee SL, Bernet VJ, Payne RJ, et al. Prediction of hypocalcemia after using 1- to 6-hour postoperative parathyroid hormone and calcium levels: an analysis of pooled individual patient data from 3 observational studies. Head Neck. 2010;32(4):427-434.
10. Lang BHH, Yih PC, Ng KK. Quick intraoperative parathyroid hormone assay at skin closure predicts clinically relevant hypocalcemia after thyroidectomy. World J Surg. 2012;36(6):1300-6.
11. Wiseman JE, Mossanen M, Ituarte PHG, Bath JMT, Yeh MW. An algorithm informed by the parathyroid hormone level reduces hypocalcemic complications of thyroidectomy. World J Surg. 2010;34(3):532-537.
12. Swift WM, Iorio CB, Hamdi OA, Mallawaarachchi I, Wages NA, Shonka DC Jr. Change in parathyroid hormone levels from baseline predicts hypocalcemia following total or completion thyroidectomy. Head Neck. 2022;44(7):1588-1595.