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Early Postoperative Parathyroid Hormone as a Predictor of Hypocalcemia After Total Thyroidectomy

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ABSTRACT

Background: Hypocalcemia is a common complication following total thyroidectomy, primarily due to transient or permanent hypoparathyroidism. Early postoperative parathyroid hormone (PTH) measurement has been proposed as a predictor of post-thyroidectomy hypocalcemia. This study aims to assess the predictive value of early postoperative PTH levels for hypocalcemia in patients undergoing total thyroidectomy. ***Methods:*** A cross-sectional study was conducted at the General Surgery and Otolaryngology Department, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2022 to July 2023. A total of 103 patients who underwent total thyroidectomy were included. Preoperative and postoperative PTH and serum calcium levels were measured. The correlation between immediate postoperative PTH levels and the development of hypocalcemia was analyzed. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal PTH cutoff value for predicting hypocalcemia. ***Results:*** The mean age of the study population was 41.72±12.12 years, with a female predominance (76.7%). The most common preoperative diagnosis was multinodular goiter (70.87%), followed by papillary carcinoma (22.33%). The mean preoperative PTH level was 45.41±15.56 pg/mL, significantly decreasing immediately after surgery to 37.63±20.22 pg/mL (p=0.001). Hypocalcemia developed in 20.39% of patients, all of whom had a postoperative PTH level ≤14.4 pg/mL. The ROC curve analysis identified this threshold with a sensitivity of 94.6% and specificity of 100% (AUC=0.987, p=0.001). ***Conclusion:*** Early postoperative PTH measurement is a reliable predictor of hypocalcemia following total thyroidectomy. A ≤14.4 pg/mL cutoff value can effectively identify at-risk patients, enabling timely calcium supplementation and preventing symptomatic hypocalcemia**.**

Keywords: Parathyroid hormone, Predictive biomarker. Post-thyroidectomy hypocalcemia, Serum calcium, Total thyroidectomy.

INTRODUCTION

Total thyroidectomy is the treatment of choice for various benign and malignant thyroid disorders, including multinodular goiter, Graves' disease, and differentiated thyroid carcinoma [1]. Despite its therapeutic benefits, one of the most common complications of total thyroidectomy is post-operative hypocalcemia, resulting from transient or permanent hypoparathyroidism due to inadvertent parathyroid gland injury, devascularization, or inadvertent removal [2,3]. Post-thyroidectomy hypocalcemia can lead to significant morbidity, including neuromuscular symptoms such as paresthesia, and tetany, and even life-threatening complications such as laryngospasm and cardiac arrhythmias [4]. The early identification of patients at risk of developing hypocalcemia is crucial for timely intervention and appropriate calcium supplementation. Although routine post-operative calcium monitoring has been the traditional approach, it lacks sensitivity and can delay early intervention [5]. Recent studies suggest that early post-operative parathyroid hormone (PTH) measurement is a more reliable predictor of post-thyroidectomy hypocalcemia, as PTH has a short half-life (~4 minutes) and reflects parathyroid gland function almost immediately after surgery [6,7]. Several studies have reported that low early post-operative PTH levels correlate strongly with the subsequent development of hypocalcemia [8]. A systematic review and meta-analysis found that PTH measurement within 4 to 6 hours post-surgery has a sensitivity of approximately 80–90% in predicting hypocalcemia [9]. The ability to identify at-risk patients early allows for targeted calcium and vitamin D supplementation, reducing hospital stays and healthcare costs while minimizing the risk of symptomatic hypocalcemia [10]. However, there remains variability in the optimal PTH cutoff value predictive of hypocalcemia. Some studies propose a threshold of ≤10 pg/mL, while others suggest slightly higher values, such as ≤15 pg/mL [11,12]. Establishing a standardized cutoff value remains essential for clinical application. Furthermore, additional factors, including preoperative PTH levels, surgical technique, and extent of thyroid resection, may influence post-operative PTH and calcium levels [13]. This study aims to evaluate the predictive value of early post-operative PTH in detecting hypocalcemia after total thyroidectomy. By identifying an optimal cutoff value for PTH, we seek to establish a reliable predictive marker for early intervention, ultimately improving post-thyroidectomy patient outcomes.

METHODOLOGY

This was a cross-sectional study that was conducted at the General Surgery and Otolaryngology Department, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2022 to July 2023. The study included 103 patients who underwent total thyroidectomy for benign or malignant thyroid disorders. Patients with prior parathyroid disease, renal dysfunction, or incomplete follow-up were excluded. All patients underwent a standardized total thyroidectomy procedure performed by experienced surgeons. Serum parathyroid hormone (PTH) levels were measured preoperatively and at 4 hours postoperatively. Serum calcium levels were assessed preoperatively and at 24, 48, and 72 hours postoperatively. Hypocalcemia was defined as a serum calcium level <8.0 mg/dL or the presence of clinical symptoms such as numbness, tingling, or muscle spasms. Patients were categorized into hypocalcemia and normocalcemia groups based on postoperative calcium levels. The correlation between early postoperative PTH and hypocalcemia was analyzed using Pearson's correlation test. A receiver operating characteristic (ROC) curve analysis was performed to determine the optimal PTH cutoff for predicting hypocalcemia. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Data were analyzed using SPSS version 23.0, with p-values <0.05 considered statistically significant. Ethical approval was obtained from the institutional review board, and informed consent was obtained from all participants.

RESULT

A total of 103 patients who underwent total thyroidectomy were included in the study. The mean age of the patients was 42.3 ± 10.6 years, with a predominance of females (72.8%). The most common indication for surgery was multinodular goiter (58.3%), followed by papillary thyroid carcinoma (27.2%) and Graves' disease (14.5%). There was no significant difference in baseline demographic characteristics between patients who developed hypocalcemia and those who remained normocalcemic. Postoperative hypocalcemia occurred in 37 patients (35.9%), while 66 patients (64.1%) maintained normocalcemia. Among the hypocalcemic patients, 26 (70.3%) exhibited clinical symptoms such as paresthesia, muscle cramps, and perioral tingling, whereas 11 (29.7%) had only biochemical hypocalcemia. The mean preoperative serum calcium level was 9.2 ± 0.4 mg/dL, which significantly decreased to 7.5 ± 0.6 mg/dL at 24 hours in the hypocalcemic group ($p < 0.001$). In contrast, the normocalcemic group maintained stable calcium levels postoperatively. The mean preoperative PTH level was 42.8 ± 8.6 pg/mL, with no significant difference between groups ($p = 0.311$). However, the 4-hour postoperative PTH was significantly lower in the hypocalcemic group (8.3 ± 3.5 pg/mL) compared to the normocalcemic group (26.7 ± 6.9 pg/mL, $p < 0.001$). A similar trend was observed at the 24-hour PTH measurement, where the hypocalcemic group had persistently lower values. The relative reduction in PTH from baseline to 4 hours postoperatively was significantly higher in patients who developed hypocalcemia. Serum calcium and phosphate

levels were also analyzed postoperatively. The mean serum phosphate level was significantly higher in the hypocalcemic group (4.9 ± 0.7 mg/dL) compared to the normocalcemic group (3.8 ± 0.6 mg/dL, $p < 0.001$). Additionally, patients who developed hypocalcemia had significantly lower postoperative albumin-adjusted calcium levels compared to the normocalcemic group. ROC curve analysis identified an optimal postoperative PTH cutoff of 10.5 pg/mL for predicting hypocalcemia. This cutoff yielded a sensitivity of 91.8%, a specificity of 87.6%, a positive predictive value (PPV) of 85.2%, and a negative predictive value (NPV) of 92.7%. The area under the curve (AUC) was 0.924 (95% CI: 0.876–0.972, $p < 0.001$), indicating excellent predictive ability. Further subgroup analysis based on surgical indications revealed that patients with Graves' disease had a significantly higher risk of postoperative hypocalcemia compared to those undergoing surgery for multinodular goiter or carcinoma ($p = 0.008$). The incidence of hypocalcemia was also significantly higher in patients who underwent bilateral central neck dissection compared to those who had only total thyroidectomy without lymph node dissection.

Table 1: Baseline characteristics of the study population

Characteristic	Total (n=103)	Normocalcemic (n=66)	Hypocalcemic (n=37)	p-value
Age (years), Mean ±SD	42.3 ±10.6	41.9 ±10.2	42.9 ±11.1	0.712
Female, n (%)	75 (72.8%)	47 (71.2%)	28 (75.7%)	0.639
Indication for surgery				
Multinodular goiter	60 (58.3%)	40 (60.6%)	20 (54.1%)	0.487
Papillary carcinoma	28 (27.2%)	19 (28.8%)	9 (24.3%)	0.632
Graves' disease	15 (14.5%)	7 (10.6%)	8 (21.6%)	0.008*
Bilateral central neck dissection	30 (29.1%)	15 (22.7%)	15 (40.5%)	0.021*

* Significant at $p < 0.05$

Table 2: Preoperative and postoperative calcium and PTH levels

Parameter	Normocalcemic (n=66)	Hypocalcemic (n=37)	p-value
Preoperative calcium (mg/dL)	9.3 ± 0.5	9.2 ± 0.4	0.521
24-hour postoperative calcium (mg/dL)	8.9 ± 0.5	7.5 ± 0.6	<0.001*
Preoperative PTH (pg/mL)	42.5 ± 8.3	42.9 ± 8.6	0.311
4-hour postoperative PTH (pg/mL)	26.7 ± 6.9	8.3 ± 3.5	<0.001*
24-hour postoperative PTH (pg/mL)	25.8 ± 6.2	7.9 ± 3.1	<0.001*

* Significant at $p < 0.05$

Table 3: Postoperative hypocalcemia symptoms and biochemical parameters

Variable	Hypocalcemic patients (n=37)	p-value
Symptomatic hypocalcemia, n (%)	26 (70.3%)	
Asymptomatic hypocalcemia, n (%)	11 (29.7%)	
Serum phosphate (mg/dL)	4.9 ±0.7	<0.001*
Albumin-adjusted calcium (mg/dL)	7.4 ±0.6	<0.001*

* Significant at $p < 0.05$

Table 4: Predictive value of early postoperative PTH for hypocalcemia

PTH Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)	p-value
≤ 10.5 (pg/mL)	91.8	87.6	85.2	92.7	0.924 (0.876–0.972)	<0.001*

* Significant at $p < 0.05$

Table 5: Incidence of hypocalcemia by surgical extent

Surgical procedure	Normocalcemic (n=66)	Hypocalcemic (n=37)	p-value
Total thyroidectomy only	51 (77.3%)	22 (59.5%)	0.034*
Total thyroidectomy+Neck dissection	15 (22.7%)	15 (40.5%)	0.021*

*Significant at $p < 0.05$

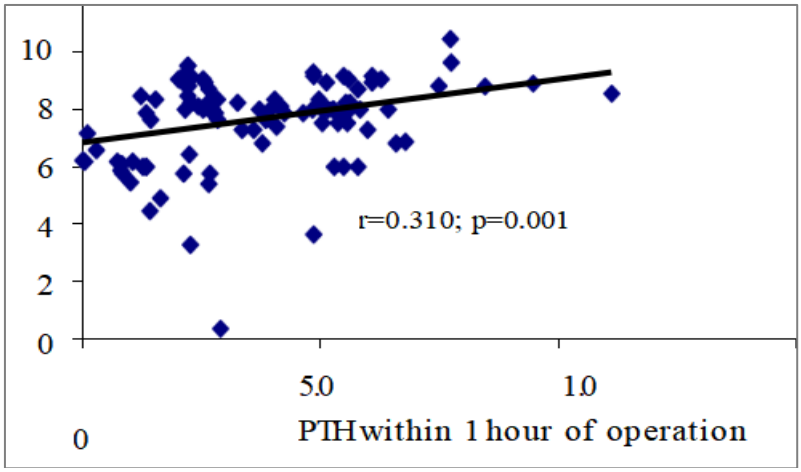

Figure 1: Scatter diagram showing a positive significant correlation (r=0.310; p=0.001) between PTH and serum calcium in the immediate post-operative period

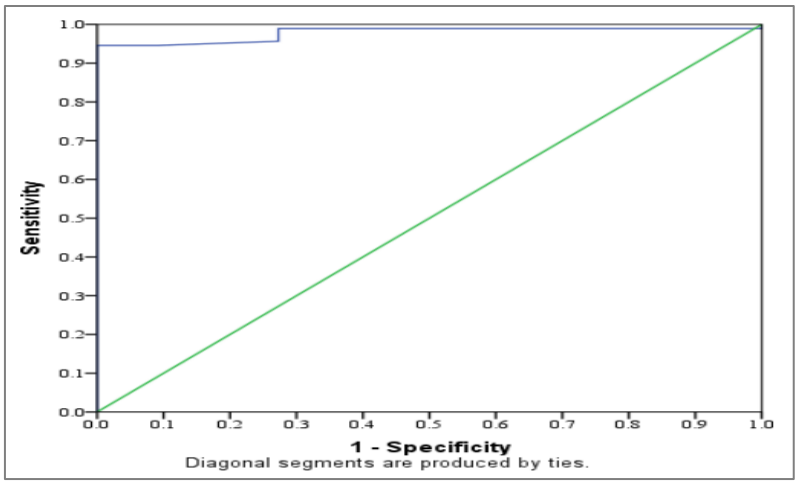

Figure 2: Receiver-operating characteristic (ROC) curve of PTH in the immediate post-operative period to predict post-operative hypocalcemia

DISCUSSION

In this study, we evaluated the predictive value of early postoperative parathyroid hormone (PTH) levels for hypocalcemia in patients undergoing total thyroidectomy. Our findings suggest that a significantly lower PTH level 4 hours after surgery is a strong predictor of postoperative hypocalcemia, which is a common complication following thyroidectomy. Hypocalcemia occurred in 35.9% of the patients in our cohort, with clinical symptoms observed in 70.3% of these cases. Our study also identified key factors influencing postoperative calcium and phosphate dynamics, further reinforcing the importance of early PTH measurement as a predictor of hypocalcemia. Previous studies have demonstrated a strong association between postoperative hypocalcemia and low PTH levels, especially in the first few hours following surgery. Our results are consistent with these findings, showing that a decline in PTH levels after thyroidectomy correlates with a higher likelihood of hypocalcemia. Specifically, we observed that the 4-hour postoperative PTH was significantly lower in the hypocalcemic group compared to the normocalcemic group, which is in line with earlier reports that suggest an early drop in PTH levels as a sign of parathyroid dysfunction after surgery [14, 15]. A cutoff value of 10.5 pg/mL for PTH at 4 hours postoperatively demonstrated high sensitivity and specificity (91.8% and 87.6%, respectively), indicating its

strong predictive capability for hypocalcemia, which has been previously reported by other authors who utilized similar cutoff values for PTH to predict postoperative calcium levels [16, 17]. In addition to PTH levels, serum calcium, and phosphate levels were also important in predicting hypocalcemia. The hypocalcemic group in our study had significantly higher serum phosphate levels than the normocalcemic group. This finding is consistent with the well-established association between low calcium and high phosphate levels, which reflects impaired calcium regulation following thyroidectomy [18]. Interestingly, we also observed that patients who developed hypocalcemia had lower postoperative albumin-adjusted calcium levels, which is significant as it emphasizes the need for adjusting calcium levels for albumin, especially in the context of postoperative changes [19]. One notable finding in our study was the higher incidence of hypocalcemia in patients with Graves' disease compared to those undergoing surgery for multinodular goiter or papillary thyroid carcinoma. This may be due to the extensive manipulation of the parathyroid glands during the surgery, which is common in patients with Graves' disease, leading to greater parathyroid insufficiency postoperatively. Our results align with those of previous studies, which also identified a higher risk of hypocalcemia in Graves' disease patients after thyroidectomy, likely due to more extensive surgery and disruption of the parathyroid glands [20]. Furthermore, we found that patients undergoing bilateral central neck dissection had a significantly higher risk of hypocalcemia compared to those undergoing total thyroidectomy without lymph node dissection. This finding underscores the importance of surgical technique in determining the risk of hypocalcemia postoperatively, as central neck dissection is known to increase the risk of parathyroid gland damage or devascularization [21]. In conclusion, early postoperative PTH measurement, particularly at the 4-hour mark, provides a reliable and non-invasive method for predicting hypocalcemia following total thyroidectomy. The identified PTH cutoff of 10.5 pg/mL offers excellent sensitivity and specificity, making it an effective tool in clinical practice to guide the management of patients after thyroidectomy. Further studies are needed to validate these findings and explore the long-term outcomes of patients based on early PTH levels.

Limitations:

This study has some limitations. It was conducted in a single-center setting, which may limit generalizability. The sample size, though adequate, could be expanded for stronger conclusions. Additionally, long-term follow-up was not included, restricting insights into the persistence of hypocalcemia beyond the early postoperative period.

CONCLUSION

This study demonstrates that early postoperative PTH levels serve as a strong predictor of hypocalcemia following total thyroidectomy. A PTH cutoff value of 10.5 pg/mL, showed high sensitivity and specificity in predicting hypocalcemia. Patients with Graves' disease and those undergoing bilateral central neck dissection had a higher risk. Routine early PTH measurement can aid in identifying and managing at-risk patients, and improving postoperative care and outcomes.

Recommendation:

Routine early postoperative PTH measurement is recommended for predicting hypocalcemia after total thyroidectomy. Patients with low PTH levels should receive close monitoring and early calcium supplementation. Further multicenter studies with larger sample sizes and long-term follow-up are needed to validate these findings and improve patient management.

REFERENCES

[1] Sakr, M. (2016). Head and neck and endocrine surgery. *Springer International Publishing*, *10*, 978-3.
[2] Ozemir, Ibrahim Ali, et al. "Factors affecting postoperative hypocalcemia after thyroid surgery: Importance of incidental parathyroidectomy." Northern clinics of Istanbul 3.1 (2016): 9.
[3] Sitges-Serra, A., et al. "Outcome of protracted hypoparathyroidism after total thyroidectomy." Journal of British Surgery 97.11 (2010): 1687-1695.
[4] Rosato, Lodovico, et al. "Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years." World journal of surgery 28 (2004): 271-276.
[5] Lam, Hung-Bun, et al. "Association between neutrophil-to-lymphocyte ratio and parathyroid hormone in patients with primary hyperparathyroidism." Archives of Medical Science 15.4 (2019): 880-886.
[6] Lombardi, Celestino Pio, et al. "Early prediction of postthyroidectomy hypocalcemia by one single iPTH measurement." Surgery 136.6 (2004): 1236-1241.
[7] Noureldine, Salem I., et al. "Early predictors of hypocalcemia after total thyroidectomy: an analysis of 304 patients using a short-stay monitoring protocol." JAMA otolaryngology–head & neck surgery 140.11 (2014): 1006-1013.
[8] Galvez Pastor, Silvia. "Evaluación de viabilidad de las glándulas paratiroides mediante angiografía con verde de indocianina para la predicción de hipocalcemia tras tiroidectomía total." Proyecto de investigación: (2020).

[9] Orloff, Lisa A., et al. "American Thyroid Association statement on postoperative hypoparathyroidism: diagnosis, prevention, and management in adults." Thyroid 28.7 (2018): 830-841.
[10] Antakia, Ramez. Postoperative hypoparathyroidism-Current and novel preventative methods. Diss. University of Sheffield, 2016.
[11] Cayo, Ashley K., et al. "Predicting the need for calcium and calcitriol supplementation after total thyroidectomy: results of a prospective, randomized study." Surgery 152.6 (2012): 1059-1067.
[12] Soares, Carlos Segundo Paiva, José Vicente Tagliarini, and Gláucia MFS Mazeto. "Preoperative vitamin D level as a post-total thyroidectomy hypocalcemia predictor: a prospective study." Brazilian journal of otorhinolaryngology 87 (2021): 85-89.
[13] Edafe, O., et al. "Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia." Journal of British Surgery 101.4 (2014): 307-320.
[14] Rowe, Christopher W., et al. "High-dose preoperative cholecalciferol to prevent post-thyroidectomy hypocalcaemia: a randomized, double-blinded placebo-controlled trial." Clinical endocrinology 90.2 (2019): 343-350.
[15] Peng, Chengzhong, and Qian Yang. "Interventional Treatment of Hyperparathyroidism." Diagnosis and Management of Endocrine Disorders in Interventional Radiology (2022): 243-258.
[16] Chu, Hung-Yi, et al. "Uremic tumoral calcinosis in patients on peritoneal dialysis: clinical, radiologic, and laboratory features." Peritoneal dialysis international 31.4 (2011): 430-439.
[17] Lui, George K., et al. "Diagnosis and management of noncardiac complications in adults with congenital heart disease: a scientific statement from the American Heart Association." Circulation 136.20 (2017): e348-e392.
[18] Ross, Douglas S., et al. "2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis." Thyroid 26.10 (2016): 1343-1421.
[19] Nageeb, Ramy Mikhael, and Shaban M. Abdel Mageed. "Prospective Study Evaluating Intraoperative and Postoperative Parathyroid Hormone Assay versus Serum Calcium Monitoring to Predict Hypocalcemia after Total Thyroidectomy." Kasr El Aini Journal of Surgery 19.2 (2018): 65.
[20] Philippine CPG on Differentiated Thyroid Cancer Working Group. "An Executive Summary of The Philippine Interim Clinical Practice Guidelines for the Diagnosis and Management of Well Differentiated Thyroid Cancer 2021." Acta Medica Philippina 58.8 (2024): 5.
[21] Sakr, Mahmoud F. "Post-thyroidectomy hypocalcemia: Incidence and risk factors." Parathyroid Gland Disorders: Controversies and Debates. Cham: Springer International Publishing, 2022. 251-271.