

Early postoperative PTH level following total thyroidectomy as a predictor of hypocalcemia: a single center-based study in Bangladesh.

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Abstract

Background: Assessment of parathyroid hormone (PTH) following thyroid surgery assists in the prediction of hypocalcemia and permits early intervention and therapy with oral calcium and/or vitamin D supplements. **Methods:** This retrospective analysis comprised 141 individuals who had undergone a total or completion thyroidectomy over the previous four years. The blood PTH level was measured 3 hours after surgery to determine its change and to predict hypocalcemia. **Results:** Patients were predominately female (75.2%), and the mean age was 48.73 ± 13.44 years. The main surgical procedure was total thyroidectomy (80.14%), and the main cause for surgery was a multinodular goiter (34.04%). A comparable number of patients with each type of thyroid disease (multinodular goiter, papillary thyroid cancer, thyroiditis, Graves' disease or toxic multinodular goiter) were enrolled. Three hours after surgery 93 patients (65.95%) had serum PTH levels of >10 pg/ml (mean 28.06) and 90 patients (68.38%) had normal serum calcium (mean 8.66). Most of these 93 patients (65.95%) didn't require postoperative supplementation, whereas 48 patients (34.05%) with serum PTH levels less than 10 pg/ml required some form of supplementation; 39 (27.65%) required both oral calcium and vitamin D supplements, and 9 (6.4%) required only oral vitamin D supplementation. There was a significant correlation between the 3-h postoperative PTH level and hypocalcemia (P -value 0.000). The type of pathology had no significant association with low serum PTH level after surgery (P -value 0.166). **Conclusion:** Asymptomatic individuals with PTH levels less than 10 pg/ml, who are regarded as being in the high-risk category, can start taking calcium and/or vitamin D supplements early if their PTH levels are measured at 3 hours following complete thyroidectomy. To predict hypocalcemia, more research is required to compare the outcome of early serum PTH level with the day one serum PTH level following complete thyroidectomy.

Keywords: Hypocalcemia, Hypoparathyroidism, parathyroid hormone PTH, Thyroidectomy, Bangladesh

Introduction: The ideal care for patients with hypocalcemia following thyroid surgery is still a subject of intense dispute, and several postoperative management protocols have been developed to obtain the best management plan and reduce the incidence of postoperative hypocalcemia. Symptomatic parathyroid dysfunction is a frequent consequence after total or complete thyroidectomy and it may be associated with severe patient morbidity following surgery, as well as prolong hospitalization and raise readmission rates^{1,2}

The parathyroid glands may be accidentally or purposely damaged or removed together with the thyroid gland during surgery; temporary ischemia or complete infarction of the gland may also result in parathyroid dysfunction. The amount of parathyroid hormone (PTH) is measured after surgery to determine iatrogenic damage to the parathyroid gland¹

This release is regulated by calcium receptors on the surface of parathyrocytes. PTH is an 84-amino acid protein secreted by the parathyroid glands, and its secretion is substantially influenced by the level of

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ionized blood calcium via a direct feedback mechanism from external calcium ions. The PTH half-life is determined in minutes and is easily measurable in serum³.

PTH is divided into a set of tiny proteins with varied half-lives and biological functions. Depending on the biological activity of the PTH particles and the amount of serum vitamin D, the onset of clinically evident hypocalcemia may take up to 48 hours following the onset of hypoparathyroidism².

Early calcium and/or vitamin D supplementation can significantly keep high-risk patients asymptomatic and prevent the development of symptomatic hypocalcemia with its associated morbidity because there is a delay between the development of hypoparathyroidism and the appearance of symptomatic hypocalcemia¹.

Some surgeons have urged the routine use of postoperative oral calcium and/or vitamin D supplements to reduce the likelihood of hypocalcemia and shorten hospital stays. In outpatient or short-stay settings, where there is little time to cure hypocalcemia once it is identified, such regular usage is particularly prevalent. Others have argued that if symptoms of hypocalcemia appear, patients should be sent home with prescriptions for elemental calcium supplements that may be completed⁴.

Following thyroid surgery, some studies advise routinely measuring parathyroid hormone levels as this can help predict the onset of hypocalcemia. Early intervention and management can prevent or at least delay the onset of such complications, allowing patients to leave the hospital sooner after surgery. It has also been demonstrated that routine use of oral calcium and/or vitamin D supplements can lower its occurrence⁵⁻⁸.

To assist surgeons in separating patients who have a low chance of developing hypocalcemia from those who require calcium supplements treatment and inpatient care, it is critical to find the most trustworthy early indicators of hypocalcemia. When compared to customary postoperative hospital stays, the capacity to discern between these groups may enable a cost savings of up to 50%.⁴

The purpose of the present investigation was to

identify independent risk factors for the development of postoperative hypocalcemia, as well as subgroups of patients at especially high or low risk. Surgeons may be able to accurately choose patients for outpatient or short-stay surgeries if they can reliably identify individuals at risk for hypocalcemia.

This study aims at assessing the effect of early postoperative estimate of parathyroid hormone in predicting the development of hypocalcemia following total thyroidectomy and treating patients with oral supplementation of calcium and vitamin D to reduce the substantial clinical hypocalcemia.

Study Design

Patients and methods

This was a retrospective study conducted between January 2020 and December 2022 at the Central Medical College in Cumilla, Bangladesh. This comprised 141 individuals who received completion or total thyroidectomy under general anesthesia at a single surgical facility. A single surgeon with experience in the fields of ENT-Laryngology and Otolaryngology performed the surgeries.

The Institution's Ethics Committee approved the protocol, and signed informed permission was acquired from all participants.

141 patients aged 27 to 71 years who underwent total and complete thyroidectomy for multinodular goiter (MNG), a suspicious nodule (PTC) on cytological examination following fine needle aspiration, Graves' disease, or toxic multinodular goiter were recruited. To statistically determine whether thyroid disease influences blood PTH levels, we enrolled an equal number of patients in each group. All patients receiving total thyroidectomy for suspicious nodules were found to have differentiated thyroid cancer by histological investigation (papillary or follicular).

Patients had severe conditions (diabetes in its advanced stage, immunological diseases, or hematological disorders) or hematological disorders. Patients under the age of 18, those who received lobectomy or less than complete thyroidectomy, and those who refused to participate were excluded from the research.

A venous sample was provided for the measurement of the PTH level 3 h following surgery. Quantitative in vitro analysis was used at a hospital laboratory to determine the PTH concentration. As a standard,

serum PTH values between 10 and 55pg/ml were considered normal. Its concentration below 10 pg/ml was considered decreased. Normal blood calcium levels range between 8.5 to 10.5 mg/dl; hypocalcemia is defined as serum calcium levels of 8.4 mg/dl or below. Before surgery, serum PTH and calcium levels were normal for all patients. After surgery, individuals whose PTH was <15 pg/mL and/or blood calcium was <8.5 mg/dL were evaluated for postoperative oral calcium and vitamin D supplements. In most cases, an oral regimen of 400–1200 mg per day of elemental calcium (1–3 g of calcium carbonate; i.e. 2–6 TUMS per day) or the equivalent in calcium citrate (2000–6000 mg per day) was adequate. Vitamin D (calcitriol, generally 0.25–0.5 mcg twice day) was added to their prescription if consecutive readings revealed a drop in blood calcium levels.

Statistical Analyses

Statistical data analysis was carried out using Excel and SPSS (version 25.0; SPSS Inc., Chicago, IL, USA). The data are presented as the mean standard deviation (SD), percentage, and frequency. Fisher's exact test was utilized to demonstrate a link between the blood PTH and several patient features. The odds ratios (OR) were presented alongside confidence intervals (CI) and P values. The statistical significance level was determined to be $p < 0.05$.

Results

Table 1 describes characteristics of the study population. Patients were predominately female (75.2%), and the mean age was 48.73 ± 13.44 years. The main surgical procedure was total thyroidectomy (80.14%), and the main cause for surgery was a multinodular goiter (34.04%).

A comparable number of patients with each type of thyroid disease (multinodular goiter, papillary thyroid cancer, thyroiditis, Graves' disease or toxic multinodular goiter) were enrolled. The MNG group was composed of 48 (34.04%) patients,

Table-1. Demographic and Clinical Characteristics of the Study Population

Category (n = 141)	Number of patients (N)	Percentage (%)
Gender		
Male	35	24.8
Female	106	75.2
Age (Mean \pm SD)	48.73 \pm 13.44	

Surgical procedure		
Total thyroidectomy	113	80.14
Completion thyroidectomy	28	19.85
Diagnosis		
MNG	48	34.04
PTC	43	30.49
Toxic MNG	22	15.6
Thyroiditis	12	8.51
Graves' disease	6	4.25
Recurrent MNG	4	2.83
Follicular carcinoma	3	2.12
Anaplastic thyroid cancer	3	2.12

Abbreviations: MNG: multinodular goiter, PTC: papillary thyroid cancer.

the PTC group was composed of 43 (30.49%) patients, and the Toxic MNG, Thyroiditis, Grave's disease, Recurrent MNG, Follicular Carcinoma and Anaplastic Thyroid cancer showed respectively (15.6%, 8.51%, 4.25%, 2.83%, 2.12% and 2.12%). (Fig.1)

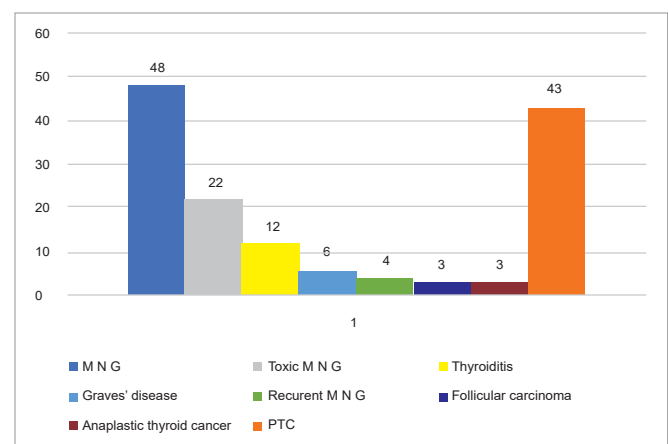


Fig-1: Pre-operative diagnosis of the study populations (n=141).

In 93 patients (65.95%) the PTH level was greater than 10 pg/ml after surgery with a mean level of 28.06, and 90 patients (63.8%) have normal serum calcium level after surgery with a mean level of 8.66. Table:2

Table 2. Showing the postoperative serum levels of the parathyroid hormone and the calcium.

Categories	Number of patients	Percentage
Serum PTH 3 h after surgery		
Normal (10–55 pg/ml)	93	65.95
Reduced (<10 pg/ml)	48	34.05
Serum calcium 24 h after surgery		
Normal (8.5–10.5 mg/dl)	90	63.8
Reduced (<8.4 mg/dl)	51	36.2

After surgery, 93 patients (65.95 %) with serum PTH levels greater than 10 pg/ml did not require any postoperative supplementation, whereas 48 patients (34.05 %) with serum PTH levels less than 10 pg/ml required some form of supplementation; 39 (27.65 %) required both oral calcium and vitamin D supplements, and 9 (6.4 %) required only oral vitamin D supplementation. Fig:2

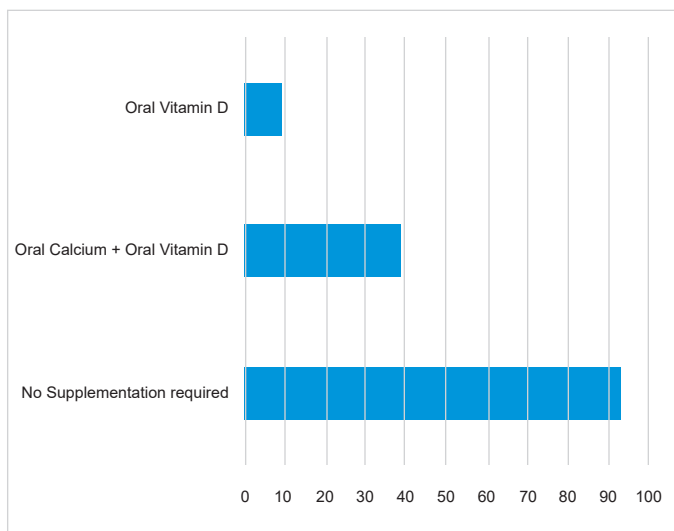


Fig-2: A basic bar chart displaying the percentages of patients that required postoperative calcium and/or vitamin D supplements.

There were substantial relationships between the 3 h postoperative blood PTH levels and the 24 h postoperative serum calcium levels, but no associations with the pathology, gender, or surgical method. Table-3

Table 3. Demonstrating the correlation between serum PTH 3 hours after surgery and various patient variables.

Variables	Serum PTH 3 h after surgery		Sig. (2-sided)
	Normal (n = 93)	Reduced (n = 48)	
Gender			0.059*
Male	24 (26%)	11 (23%)	
Female	69 (74%)	37 (77%)	
Surgical procedure			0.237*
Total thyroidectomy	80 (86%)	33 (69%)	
Completion thyroidectomy	13 (14%)	15 (31%)	
Serum calcium 24 h after surgery			0.000*
Normal	74 (82%)	0 (0.0%)	
Reduced	16 (18%)	51 (100%)	
Diagnosis			0.166*
MNG	30 (32%)	18 (38%)	
Recurrent MNG	3 (3%)	1 (2%)	
Toxic MNG	18 (20%)	4 (8.3%)	
Graves' disease	4 (4%)	2 (4.1%)	
PTC	28 (30%)	15 (31%)	
Anaplastic thyroid cancer	2 (2%)	1 (2%)	
Thyroiditis	8 (9%)	4 (8.4%)	
Follicular Carcinoma	0 (0.0%)	3 (6.2%)	

*Fischer Exact test.

Discussion

Thyroid cancer, symptoms such as tracheal tightness or trouble swallowing, or thyroid malfunction including the synthesis of excess thyroid hormone (e.g., toxic nodule, toxic multinodular goiter, and Graves' disease) are the most common reasons for thyroidectomy. Although thyroidectomy is today regarded as a fairly safe procedure, recognized consequences can severely impair patients' quality of life⁹. The most frequent adverse events following thyroidectomy are postoperative bleeding, recurrent laryngeal nerve damage (RLN), and hypocalcemia. The risk of postoperative hypocalcemia is the subject of this investigation. In fact, this is the most common complication of thyroid surgery, with a frequency of up to 50% following complete thyroidectomy¹⁰⁻¹⁵.

Post-thyroidectomy hypocalcemia is usually transitory, although it might develop permanent in rare cases. It can result in significant symptoms and lengthen hospitalization. As a result, prevention is a primary focus of thyroid surgery. As previously stated, hypocalcemia is caused by hypoparathyroidism

as a result of parathyroid gland damage, removal, or unintentional devascularization during surgery¹⁶.

It is still unclear whether PTH testing following thyroid removal is most effective for properly predicting post-operative hypocalcemia. PTH has a short half-life, which is widely known. During parathyroid surgery, serum PTH is routinely measured within 10 minutes after the parathyroid is removed. However, recent research indicates that PTH testing 3 to 4 hours after thyroidectomy may be the most effective time to predict post-operative hypocalcemia^{17,18}.

Vitamin D is a fat-soluble vitamin that has a significant influence on blood calcium levels; its pharmacokinetics to elevate serum calcium levels may need up to 48 hours. It is crucial to identify high-risk individuals with hypoparathyroidism and hypocalcemia following thyroid surgery in order to supplement them with calcitriol as soon as possible. The PTH is measured 3 hours after surgery, and blood calcium is measured 24 hours after surgery¹. Nevertheless, a research conducted in Bangladesh revealed a link between immediate post-operative PTH levels and the development of hypocalcaemia 24 and 48 hours following complete thyroidectomy¹⁹.

The range of a normal PTH level is thought to be between 10 and 55 pg/ml. The mean PTH level of the patients in the current research was 28.06 pg/ml, and 3 hours after surgery, 34.05% of the patients were found to have low PTH levels. Studies suggest that transitory hypoparathyroidism can be diagnosed in up to 65 % following whole or complete thyroidectomy, although the risk of irreversible malfunction can reach up to 3–5 %. The intraoperative measurement of PH is not more important than the postoperative PTH test. PTH levels are dramatically lowered three hours following a thyroidectomy, hence many published publications propose measuring PTH at this time point^{20,21}.

The absence of a significant correlation between the kind of disease and the development of low serum PTH following surgery (P-value = 0.166) may be attributable to the essentially same surgical approach. Thyroid cancer cases typically need a more thorough dissection and may be associated with a greater frequency of parathyroid damage^{22,23}.

Our patients' mean serum calcium level was 8.695 mg/dl, and 51 patients (36.2%) were identified as

having hypocalcemia, which is defined as serum calcium levels below 8.5 mg/dl. We observed a significantly lower rate of hypocalcemia when compared with similar papers, although the number of our patients is not particularly great. Studies had revealed that hypocalcemia is the most common complication following total thyroidectomy, with a rate reaching up to 25% after surgery within 24 hours²⁴.

24 hours after surgery, there was a strong association between the 3 h postoperative PTH level and the onset of hypocalcemia (P-value 0.000). The development of hypocalcemia may be predicted by a single test of PTH levels after surgery, and early calcium and vitamin D administration will stop the onset of clinically severe hypocalcemia and may subsequently lower readmission rates. Some authors advocate repeated PTH monitoring within 18 h following thyroidectomy²⁵⁻²⁷.

Although it has been shown that low PTH levels after surgery are related with symptomatic hypocalcemia, the authors emphasize that additional research is necessary to determine the PTH threshold that indicates medical therapy with calcium supplements or vitamin D. Other studies determined that PTH may not be the sole component in the development of hypocalcemia, and that other variables may play a significant role.

Conclusion

In asymptomatic individuals with a PTH level of less than 10 pg/ml, who are at a high risk of developing hypocalcemia, PTH measurements 3 hours after a complete thyroidectomy are an accurate predictor of hypocalcemia and allow for the early start of calcium and vitamin D supplementation. Additionally, it enables the safe and prompt (2nd postoperative day) release of patients with PTH levels greater than 10 pg/ml without the need for extra calcium supplements. In order to predict hypocalcemia, more research is required to compare the outcome of early serum PTH level with day one serum PTH level following complete thyroidectomy.

Declarations

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Ethical Approval

The ethical permission received from the ethics review committee of Central medical college. Prior to data collection, patients were told about the project and consented, and anonymity was maintained throughout the study by removing their names and other personal identifiers. Confidentiality was strictly maintained during data processing and report writing.

Consent to participate

All procedures performed in this study followed the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all the enrolled patients.

Consent for Publication: Not applicable

Code Availability: Not applicable

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