

# Post Thyroidectomy Assessment of Intact Parathyroid Hormone for Early Prediction of Hypocalcaemia

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## Abstract

**Background:** As the half-life of intact parathyroid hormone (iPTH) is very low, it reflects parathyroid insufficiency within minutes to hours after total thyroidectomy. Therefore, iPTH level assessment in the postoperative period can be used to predict the development of hypocalcaemia. The optimal time point to measure serum iPTH is important for the accurate prediction of hypocalcaemia. **Aim:** This paper aims to evaluate the ability of iPTH as an early predictive marker of hypocalcaemia and determine which time iPTH is more able to predict postoperative hypocalcaemia. **Method:** This prospective observational study was conducted in the Department of Otolaryngology-Head & Neck Surgery, BSMMU, Dhaka, from July 2020 to December 2021, with 67 patients who underwent total thyroidectomy. iPTH levels were measured on the day before the operation and at 1 hour, 4 hours, and 24 hours after the operation. S.calcium levels were measured on the day before the operation and 1<sup>st</sup> postoperative day. All the data were compiled and sorted properly and were analyzed statistically. **Results:** Postoperative hypocalcaemia developed in 18 cases, with an incidence of 26.9%. Pearson correlation showed a significant correlation between postoperative iPTH at 1 hr, 4 h, and 24 hr with 1st postoperative calcium value. The Receiver operating characteristic (ROC) curve was processed for the postoperative iPTH at 1 hr, 4 h, and 24 hr. The sensitivity, specificity, cut-off value, and mean AUC found 93.9%, 94.4%,

≤14.0, 0.988; 95.9%, 94.4%, ≤09.5, 0.993 and 91.8%, 94.4%, ≤11.0, 0.993 respectively. **Conclusion:** iPTH can be used as an early predictor of post-thyroidectomy hypocalcaemia. 4 hr iPTH showed more sensitivity and specificity for a cut-off value near the laboratory reference range.

### Keywords

Total Thyroidectomy, Hypocalcaemia, Serum Intact Parathyroid Hormone, Early Predictor of Hypocalcaemia

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## 1. Introduction

Total thyroidectomy is currently one of the standard surgical procedures for the management of several malignant and benign thyroid diseases. Hypocalcaemia from postoperative hypoparathyroidism is one of the common complications of total thyroidectomy [1]. The position and number of parathyroids in the human body are variable. This variation makes identification and preservation of the parathyroid glands during surgery very challenging [2].

Hypocalcaemia after total thyroidectomy remains a challenging problem despite progress in surgical technique and even in the most experienced hands. The reported prevalence is 3% to 52% for transient and 0.4% to 13% for permanent hypocalcemia [3] [4].

The most common cause of acquired hypoparathyroidism is secondary to trauma or surgery to the thyroid, parathyroid, or neck [5]. During surgery, damage to the parathyroid glands may occur due to gland devascularization, mechanical and thermal trauma, or inadvertent removal of the parathyroid gland with the thyroid lobe. All these factors lead to a transient or permanent reduction in the functional parathyroid parenchyma [6]. Postoperative alkalosis-induced hypocalcaemia resulting from hyperventilation, triggered by postoperative pain, and dilution hypocalcaemia should also be taken into aetiological consideration [7].

Calcium metabolism is a key element in the maintenance of cellular homeostasis. Deficiency may be expressed as confusion, nausea, vomiting, and tingling in the extremities and around the mouth. Even more seriously, convulsions or cardiac arrhythmias may occur [8]. Serum calcium is present in our body in both bound and free ion forms. Most of the bound form binds with albumin. Therefore, after parathyroid gland injury or parathyroid insufficiency, it takes time for the serum calcium level to fall. So, the signs and symptoms of hypocalcaemia may appear very late [9].

It requires 24 - 72 hours or longer after the operation to express signs and symptoms of hypocalcaemia [10]. For that reason, after thyroid surgery, it is common practice to monitor patients for clinical signs or symptoms of hypocalcaemia and to assess serum calcium levels regularly. This may require a prolonged hospital stay for the patient, consequently leading to increased healthcare

costs [11].

If it could determine which patients would become hypocalcemic within a few hours of completing thyroidectomy, then earlier management and discharge decisions could be made. Therefore, A simple, reliable test for differentiating patients who require monitoring and calcium replacement from those who are suitable for early discharge can minimize the costs of unnecessarily prolonged hospital stays and unnecessary supplementation [12] [13].

More recently, postoperative surveillance of intact parathyroid hormone (iPTH) has received much attention as an early predictive marker of post-thyroidectomy hypocalcaemia [14]. The iPTH assay reacts with both 1 - 84 PTH and 7 - 84 PTH. It can also detect other large truncated fragments of non-1 - 84 PTH. On the other hand, the whole PTH assay is specific for 1 - 84 PTH [15]. Additionally, iPTH has a half-life of approximately 2 - 5 minutes and a very rapid turnover. All these factors make it an excellent marker of parathyroid function. The decrease in iPTH precedes the decline in calcium [16].

Several previous studies have shown that decreased iPTH levels can reliably predict postthyroidectomy hypocalcaemia [17] [18]. Only a few studies have been performed to determine the optimal time to measure iPTH within 24 hours after thyroidectomy, which can more accurately predict hypocalcaemia [14].

The purpose of this study was to evaluate the ability of iPTH as an early predictive marker of hypocalcaemia and determine which time iPTH is more able to predict postoperative hypocalcaemia to obtain a safe and earlier hospital discharge.

## 2. Material and Methods

**Type of study:** Prospective observational study.

**Place of study:** Department of Otolaryngology–Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh.

**Period of study:** 18 months (July 2020 to December 2021).

**Study population:** Patients who underwent total thyroidectomy.

**Sampling technique:** Purposive sampling.

**Sample size:** 67 samples were taken.

### 2.1. Objectives

**General objectives:**

To assess serum intact parathyroid hormone (iPTH) for early prediction of hypocalcaemia following total thyroidectomy.

**Specific objectives:**

To investigate hypoparathyroidism by measuring serum iPTH level at 1 hour, 4 hours, and 24 hours after the operation;

To observe hypocalcaemia by measuring serum calcium level on the day after the operation;

To evaluate the ability of iPTH as an early predictive marker of hypocalcaemia;  
To determine which time iPTH is more able to predict postoperative hypocalcaemia.

## 2.2. Selection Criteria

### **Inclusion criteria:**

Patients who were admitted to the Department of Otolaryngology & Head-Neck Surgery at BSMMU, Shahbag, Dhaka, for total thyroidectomy.

### **Exclusion criteria:**

Lobectomy, isthmusectomy, completion thyroidectomy; Total thyroidectomy with neck dissection; Concomitant thyroiditis such as Grave's disease; Hashimoto's thyroiditis; Parathyroid adenoma, primary and secondary hyperparathyroidism; Previous neck irradiation; History of other malignancies; Chronic endocrine, metabolic disease; Kidney disease; Concurrent supplementation with calcium before the operation; Concurrent supplementation with vitamin D before the operation; Patients with medications known to affect PTH, calcium, and vitamin D levels; Ex: oral glucocorticoids, estrogen, diuretics, etc.

## 2.3. Study Variables

**Demographic variables:** Age, Gender.

**Clinical variables:** Serum calcium level, serum intact parathyroid hormone level.

**Outcome variables:** Hypocalcaemia, Hypoparathyroidism.

**Confounding variables:** To minimize the biased interpretation of the data during analysis, confounding variables, which may distort the study result, are considered. Associated thyroiditis is the anatomical variation of the parathyroid gland. The size of thyroid swelling is a confounding variable.

## 2.4. Ethical Clearance

Before starting this study, the research protocol was approved by the institutional review board (IRB) of BSMMU. Informed consent was obtained from all patients for being included in the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national).

## 2.5. Procedure

Patients admitted to the department with thyroid swelling and who fulfilled the inclusion and exclusion criteria were recruited as subjects in the study. After the selection of the subjects, the nature, purpose, and benefit of the study were explained to the patient and guardian in detail. They were encouraged to participate voluntarily. They were allowed to withdraw from the study at any time. Informed written consent was obtained from the participants. A detailed history was taken. A thorough ENT examination, including thyroid gland examination

and related systemic examinations, was performed. Preoperative arrangement and investigation, such as thyroid function test, USG of the thyroid, FNAC, preoperative S.calcium, and iPTH level, and other investigations for general anaesthesia were done. After completing the necessary procedure for the operation, the patient underwent total thyroidectomy. Detailed operation findings were noted. Intact parathyroid hormone levels were measured on the day before the operation and at 1 hr, 4 hrs, and 24 hrs after the operation. The reference interval for iPTH in the laboratory was 11 to 67 pg/mL. The S.calcium level was measured on the 1<sup>st</sup> postoperative day. The reference interval for calcium in the laboratory was 8.3 - 10.6 mg/dL. All the information was recorded in a prefixed questionnaire.

## 2.6. Data Processing and Analysis

All the data were compiled and sorted properly, and the data were analyzed statistically by using SPSS<sup>®</sup> version 26 (Statistical Program for Social Sciences, IBM Corporation, New York, USA). The summarized data were presented in the form of tables and graphs. Categorical variables were present as frequencies and percentages, and continuous variables as mean  $\pm$  SD. The qualitative data was analyzed by percentage (%) and ratio. Student's t-tests were used to compare differences between preoperative and postoperative data. For all analytical tests, p values < 0.05 were considered statistically significant. Independent samples' T-test was done to compare the mean of postoperative iPTH with first postoperative day calcium status. Pearson correlation test (Bivariate) was performed to assess the difference between first postoperative calcium and postoperative iPTH. Linear Regression analysis was done to correlate postoperative iPTH with first postoperative calcium values. Specificity, sensitivity, and cut-off values were calculated by receiver operating characteristic (ROC) for various time points of iPTH as a predictor of hypocalcaemia.

## 3. Results

A total of 67 participants underwent total thyroidectomy. Among the participants, males were 15 (22.4%), and females were 52 (77.6%), with a ratio of Male: Female = 1:3.46. The mean age of participants was  $40.49 \pm 12.100$  years, ranging from 17 to 66 years.

Among 67 participants, 39 (58.2%) patients were found to have benign diseases, and 28 (41.8%) patients were treated for malignant diseases.

Postoperative hypocalcaemia developed in 18 cases, with an incidence of 26.9% (**Table 1**).

Out of 18 hypocalcemia samples, 06 (08.9%) patients suffered from benign diseases, and 12 (17.9%) patients suffered from malignant thyroid diseases (**Table 2**).

Out of 18 hypocalcemia samples, 14 underwent total thyroidectomy without central neck dissection, and 04 patients underwent total thyroidectomy with central neck dissection.

In the preoperative period, the mean value of S.Calcium was found  $9.342 \pm 0.4961$  mg/dl, and on 1<sup>st</sup> postoperative day, the mean value was  $8.676 \pm 1.1514$  mg/dl. There was found a significant difference between preoperative and postoperative calcium levels ( $p < 0.05$ ) (**Table 3**).

Out of 67 patients, the preoperative mean value of iPTH was  $35.63 \pm 10.417$  pg/ml, and the postoperative mean values of 1 hr iPTH, 4 hr iPTH, and 24 hr iPTH were  $30.34 \pm 17.223$  pg/ml,  $28.94 \pm 17.331$  pg/ml,  $29.18 \pm 18.687$  pg/ml respectively, which shows a relative decrease in postoperative iPTH. There found a significant difference ( $p < 0.05$ ) (**Tables 4-6**).

In the case of Postoperative iPTH 1 h, among 50 normal parathyroid hormone patients, 47 were normocalcemic, and 03 were hypocalcemic. And among 17 hypoparathyroidism patients, 15 were hypocalcemic, and 02 were normocalcemic. In the case of Postoperative iPTH 4 h, among 47 normal parathyroid hormone patients, 46 were normocalcemic, and 01 were hypocalcemic. And among 20 hypoparathyroidism patients, 17 were hypocalcemic, and 03 were normocalcemic. In the case of Postoperative iPTH 24 h, among 47 normal parathyroid hormone patients, 46 were normocalcemic, and 01 was hypocalcemic. And among 20 hypoparathyroidism patients, 17 were hypocalcemic, and 03 were normocalcemic (**Table 7**).

A significant correlation was found between postoperative 1 hr, 4 hr, 24 hr, iPTH levels, and development of hypocalcemia on 1st POD of total thyroidectomy (**Table 8**).

**Table 1.** Frequency of postoperative hypocalcaemia in the study populations: (n = 67).

|               | Frequency (n) | Percentage (%) |
|---------------|---------------|----------------|
| Normocalcemia | 49            | 73.1%          |
| Hypocalcemia  | 18            | 26.9%          |

**Table 2.** Frequency of hypocalcaemia according to preoperative diagnosis (n = 67).

| Diagnosis | Calcium level at 1st POD |        |                |
|-----------|--------------------------|--------|----------------|
|           |                          | Number | Percentage (%) |
| Benign    | Normocalcemia            | 33     | 49.2%          |
|           | Hypocalcemia             | 06     | 08.9%          |
| Malignant | Normocalcemia            | 16     | 23.9%          |
|           | Hypocalcemia             | 12     | 17.9%          |

**Table 3.** Comparison of Pre and postoperative S. Calcium level of the study subjects (n = 67).

| S. Calcium (mg/dl)                              | Mean $\pm$ SD      | Median | Min - Max  | p-value |
|---|--------------------|--------|------------|---------|
| Preoperative S. Calcium                         | $9.342 \pm 0.4961$ | 9.300  | 8.5 - 10.6 | <0.05   |
| Postoperative S. Calcium at 1 <sup>st</sup> POD | $8.676 \pm 1.1514$ | 9.100  | 6.1 - 10.4 |         |

**Table 4.** Comparison of preoperative iPTH and postoperative 1 hr iPTH (n = 67).

| S. iPTH (pg/ml)         | Mean ± SD      | Median | Min - Max | p-value |
|-------------------------|----------------|--------|-----------|---------|
| Preoperative iPTH       | 35.63 ± 10.417 | 36.00  | 14 - 56   | <0.05   |
| Postoperative iPTH 1 hr | 30.34 ± 17.223 | 37.00  | 04 - 55   |         |

**Table 5.** Comparison of preoperative iPTH and postoperative 4 hr iPTH (n = 67).

| S. iPTH (pg/ml)         | Mean ± SD      | Median | Min - Max | p-value |
|-------------------------|----------------|--------|-----------|---------|
| Preoperative iPTH       | 35.63 ± 10.417 | 36.00  | 14-56     | <0.05   |
| Postoperative iPTH 4 hr | 28.94 ± 17.331 | 36.00  | 3-55      | <0.05   |

**Table 6.** Comparison of preoperative iPTH and postoperative 24 hr iPTH (n = 67).

| S. iPTH (pg/ml)          | Mean ± SD      | Median | Min - Max | p-value |
|--------------------------|----------------|--------|-----------|---------|
| Preoperative iPTH        | 35.63 ± 10.417 | 36.00  | 14 - 56   | <0.05   |
| Postoperative iPTH 24 hr | 29.18 ± 18.687 | 38.00  | 03 - 54   | <0.05   |

**Table 7.** Frequencies of 1st POD calcium status in postoperative iPTH at several time intervals (n = 67).

|                         |                            | Calcium status at 1 <sup>st</sup> POD (n) |              |       |
|-------------------------|----------------------------|---|--------------|-------|
|                         |                            | Normocalcemia                             | Hypocalcemia | Total |
| Post-operative iPTH 1 h | Normal Parathyroid Hormone | 47  | 03           | 50    |
|                         | Hypoparathyroidism         | 02  | 15           | 17    |
| Postoperative iPTH 4 h  | Normal Parathyroid Hormone | 46  | 01           | 47    |
|                         | Hypoparathyroidism         | 03  | 17           | 20    |
| Postoperative iPTH 24 h | Normal Parathyroid Hormone | 46  | 01           | 47    |
|                         | Hypoparathyroidism         | 03  | 17           | 20    |

**Table 8.** Comparative study between postoperative iPTH with 1st postoperative day S. calcium (n = 67).

|                          |               | Calcium level at 1st POD | Number | Mean ± SD      | P-value |
|--------------------------|---------------|--------------------------|--------|----------------|---------|
| Postoperative iPTH 1 h   | NORMOCALCEMIA |                          | 49     | 38.63 ± 11.977 | <0.05   |
|                          | HYPOCALCEMIA  |                          | 18     | 7.78 ± 3.059   | <0.05   |
| Post-operative iPTH 4 h  | NORMOCALCEMIA |                          | 49     | 37.20 ± 12.290 | <0.05   |
|                          | HYPOCALCEMIA  |                          | 18     | 6.44 ± 2.640   | <0.05   |
| Post-operative iPTH 24 h | NORMOCALCEMIA |                          | 49     | 38.08 ± 13.315 | <0.05   |
|                          | HYPOCALCEMIA  |                          | 18     | 4.94 ± 2.209   | <0.05   |

The result is expressed as mean ± SD.

A bivariate Pearson correlation test was done to correlate postoperative iPTH 1 hr, 4 hr, and 24 hr with 1st postoperative calcium. The r value was found 0.822, 0.805, and 0.814, respectively, which is statistically significant (p < 0.05) (**Table 9**).

**Table 9.** Correlation between postoperative iPTH with first postoperative calcium values (n = 67).

|                                     |                        | Postoperative<br>iPTH 1 h | Postoperative<br>iPTH 4 h | Postoperative<br>iPTH 24 h | Calcium level<br>at 1st POD |
|-------------------------------------|------------------------|---------------------------|---------------------------|----------------------------|-----------------------------|
| <b>Postoperative<br/>iPTH 1 h</b>   | Pearson Correlation(r) | 1                         | 0.938**                   | 0.923**                    | 0.822**                     |
|                                     | P-Value                |                           | <0.05                     | <0.05                      | <0.05                       |
| <b>Postoperative<br/>iPTH 4 h</b>   | Pearson Correlation(r) | 0.938**                   | 1                         | 0.957**                    | 0.805**                     |
|                                     | P-Value                | <0.05                     |                           | <0.05                      | <0.05                       |
| <b>Postoperative<br/>iPTH 24 h</b>  | Pearson Correlation(r) | 0.923**                   | 0.957**                   | 1                          | 0.814**                     |
|                                     | P-Value                | <0.05                     | <0.05                     |                            | <0.05                       |
| <b>Calcium level<br/>at 1st POD</b> | Pearson Correlation(r) | 0.822**                   | 0.805**                   | 0.814**                    | 1                           |
|                                     | P-Value                | <0.05                     | <0.05                     | <0.05                      |                             |

\*\*Correlation is significant at the 0.05 level (2-tailed); r = Correlation coefficient.

#### 4. Discussion

This prospective observational study was conducted in the Department of Otolaryngology-Head & Neck Surgery, BSMMU, Dhaka, from July 2020 to December 2021, with 67 patients who underwent total thyroidectomy. In this study group, out of 67 participants, males were 15 (22.4%), and females were 52 (77.6%), with a ratio of Male: Female = 1:3.46. The mean age of participants was  $40.49 \pm 12.100$  years, ranging from 17 to 66 years. Similar sex distribution had been reported by Inversin *et al.* where among 260 patients, 205 were female (78.8%), and 55 were male (21.2%), with a ratio of Male: Female = 1:3.72. Islam *et al.* (2012) reported that the mean age was  $39 \pm 13.18$  with a range of 15 to 75 years, and their study also found females predominant, with males 22.5% and females 77.5% [18]. Espino *et al.* found the mean age was  $53 \pm 14$  years. Among them, 82% of patients were female [16]. Suwannasarn *et al.* reported that 86.2% were female, with a mean age of  $43 \pm 15$  years. In their studies, female was a major victim of thyroid diseases with a mean age close to our study [1]. So, our observations regarding gender and mean age are consistent with the others.

Among 67 participants, 39 (58.2%) patients were found benign diseases, and 28 (41.8%) patients were treated for malignant diseases. 36 (53.7%) patients suffered from benign multinodular goitre, and 28 (41.8%) patients had papillary carcinoma of the thyroid. Follicular lesions were found in 03 (4.5%) patients. Schlottmann *et al.* found among 106 patients, papillary carcinoma was identified in 62 patients (58.4%) and multinodular goitre in 30 (28.3%) [8]. In their study, there were more malignant patients than in our study. Docimo *et al.* found among 328 total thyroidectomy patients, benign and malignant diseases were 83% and 17%, respectively [19]. In their study, there were more benign patients than in our study.

The incidence of biochemical hypocalcaemia was 26.9% in the study patients. Postoperative hypocalcaemia developed in 18 cases (Table 1). Cannizzaro *et al.* found in their study that the incidence of hypocalcemia was 32.2% (111 of 345



patients) [17]. Islam *et al.* in their study, the incidence of hypocalcaemia was 38.5%, and postoperative hypocalcaemia was found in 25 cases [9]. Kim *et al.* found 46% hypocalcaemia in their study [20]. Canu *et al.* and Al Khadem *et al.* reported that the prevalence of hypocalcemia is 3% to 52%. So, the incidence of hypocalcemia in our study is consistent with the others [3] [4].

In this study, out of 18 hypocalcemia samples, 06 (08.9%) patients suffered from benign diseases, and 12 (17.9%) patients suffered from malignant thyroid diseases (Table 2). Among 67 total thyroidectomies, ten subjects underwent total thyroidectomy with neck dissection. Out of 18 hypocalcemia samples, 14 underwent total thyroidectomy without central neck dissection, and 04 patients underwent total thyroidectomy with central neck dissection.

In the preoperative period, the mean value of S.Calcium was found  $9.342 \pm 0.4961$  mg/dl, and on 1st postoperative day, the mean value was found  $8.676 \pm 1.1514$  mg/dl. There was found a significant difference between preoperative and postoperative calcium levels ( $p < 0.05$ ) (Table 3). Azadbakht *et al.* also found a similar result. In their study, the mean preoperative calcium levels were  $8.8 \pm 0.5$  mg/dL, whereas serum calcium after 24 hours of the surgery was  $8.5 \pm 0.49$  mg/dL [21].

In the study group, out of 67 patients, the preoperative mean value of iPTH was  $35.63 \pm 10.417$  pg/ml, and postoperative mean values of 1 hr iPTH, 4 hr iPTH, and 24 hr iPTH were  $30.34 \pm 17.223$  pg/ml,  $28.94 \pm 17.331$  pg/ml,  $29.18 \pm 18.687$  pg/ml respectively, which shows relative decrease of postoperative iPTH. There was a significant difference ( $p < 0.05$ ) (Tables 4-6).

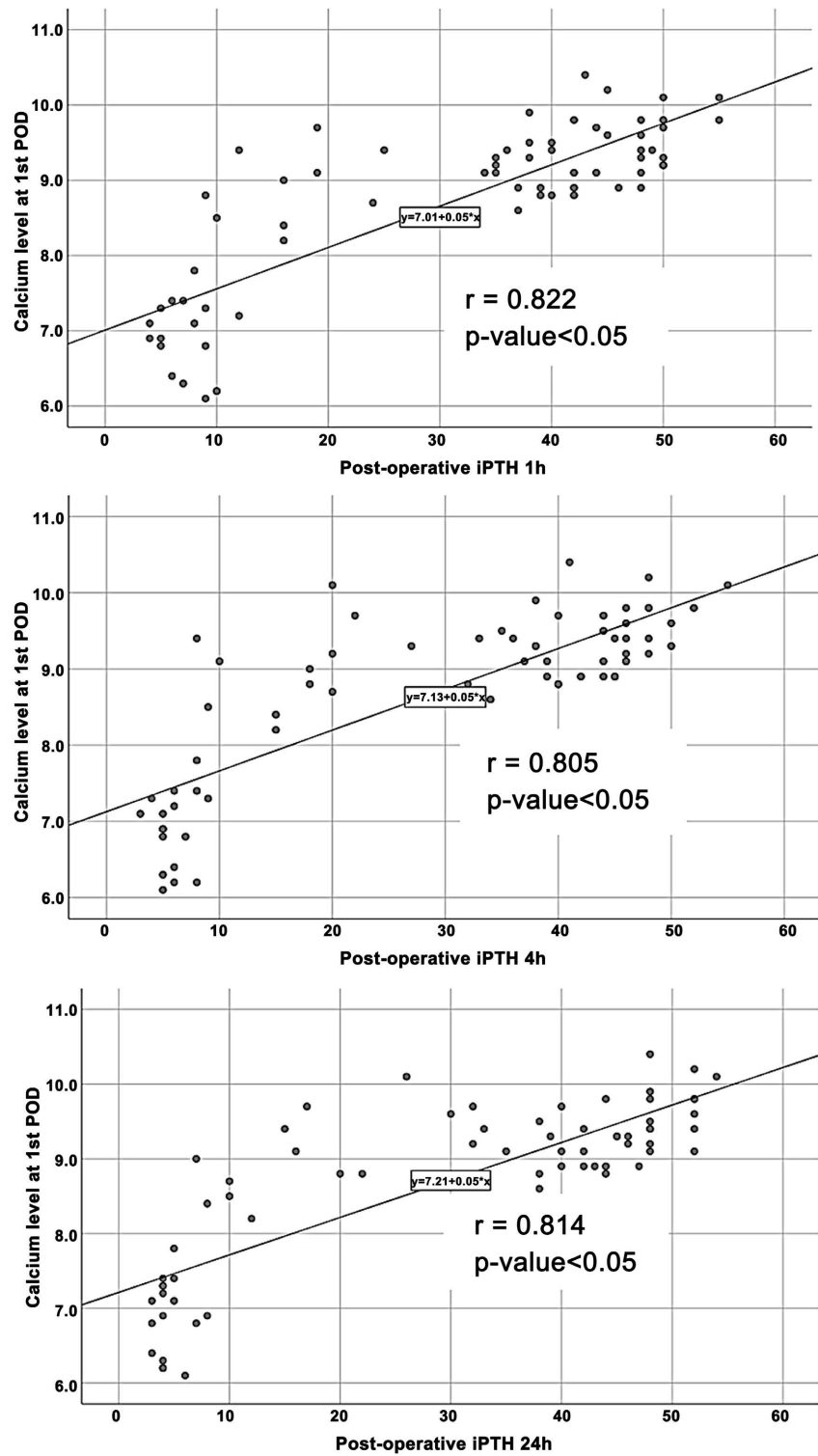
This study found, in the case of Postoperative iPTH 1 h, among 50 normal parathyroid hormone patients, 47 were normocalcemic and 03 were hypocalcemic. And among 17 hypoparathyroidism patients, 15 were hypocalcemic, and 02 were normocalcemic. In the case of Postoperative iPTH 4 h, among 47 normal parathyroid hormone patients, 46 were normocalcemic, and 01 were hypocalcemic. And among 20 hypoparathyroidism patients, 17 were hypocalcemic, and 03 were normocalcemic. In the case of Postoperative iPTH 24 h, among 47 normal parathyroid hormone patients, 46 were normocalcemic, and 01 were hypocalcemic. And among 20 hypoparathyroidism patients, 17 were hypocalcemic, and 03 were normocalcemic (Table 7).

Postoperative iPTH levels were assessed in 1 hr, 4 hr, 24 hr after operation and compared with 1st POD S.calcium level. A significant correlation was found between postoperative 1 hr, 4 hr, 24 hr, iPTH levels and development of hypocalcemia 1st POD of total thyroidectomy (Table 8).

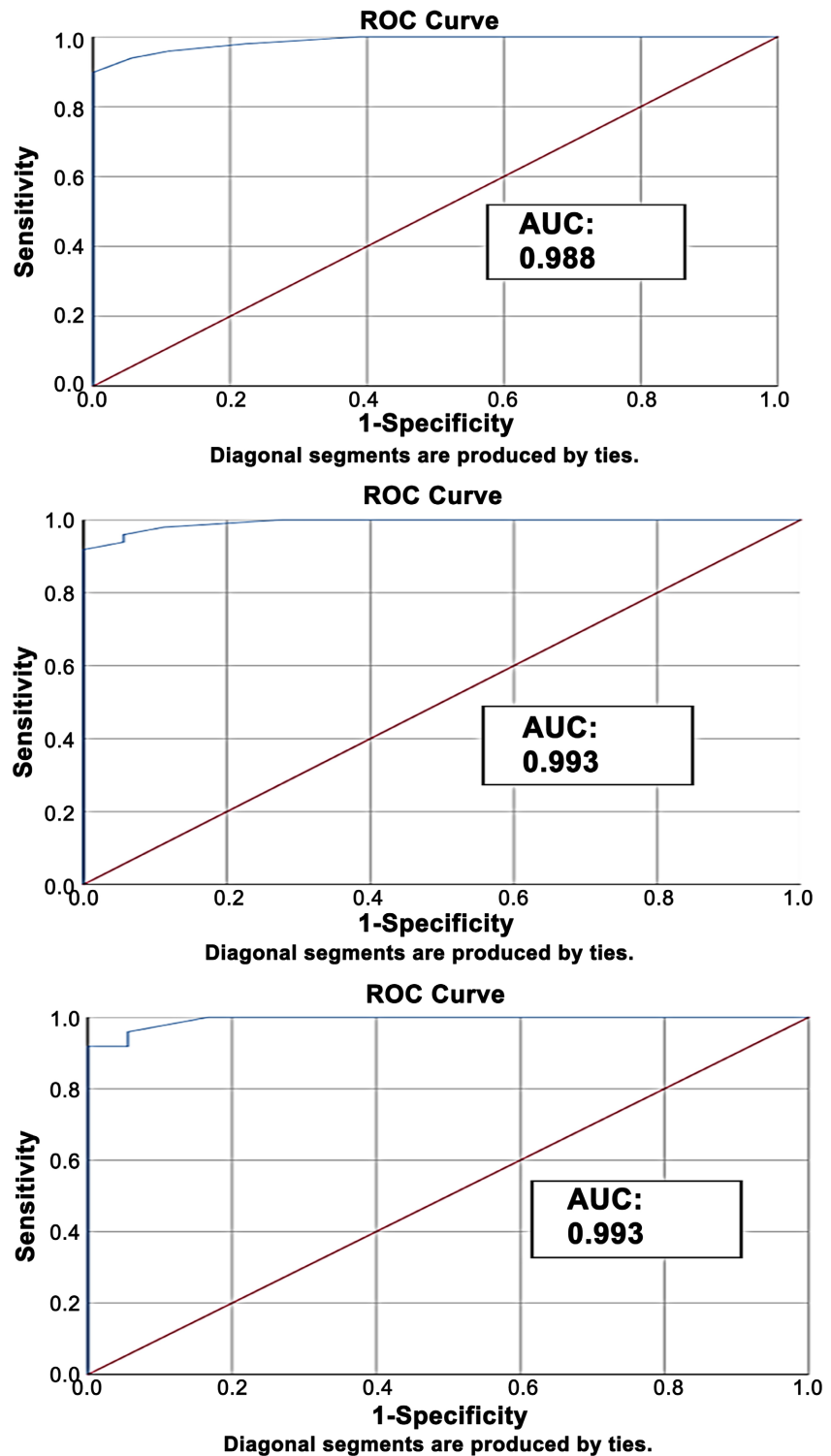
In correlating postoperative iPTH 1 hr, 4 hr, and 24 hr with 1st postoperative calcium, a bivariate pearson correlation test done. The r value was found 0.822, 0.805, and 0.814, respectively. Which is statistically significant ( $p < 0.05$ ) (Table 9).

Linear regression analysis was done to see the relation between postoperative iPTH and 1st postoperative calcium status, where postoperative iPTH was the independent variable and 1st postoperative day calcium was the dependent va-

riable. The postoperative 1 hr, 4 hr, 24 hr values were statistically significant ( $p < 0.05$ ). Those are shown as scatter diagrams (**Figure 1**).



**Figure 1.** Scatter diagram shows the correlation between postoperative iPTH 1 hr, iPTH 4 hr, iPTH 24 hr, and serum Calcium in the immediate postoperative period. ( $r$  = Correlation coefficient)



**Figure 2.** Receiver operating characteristic (ROC) curve of iPTH in 1 hr, 4 hr, 24 hr postoperative period to predict postoperative hypocalcemia of the study patients. (n = 67). AUC = Area Under The ROC Curve.

The scatter diagrams showed a positive significant correlation between post-operative different time iPTH and 1st POD serum calcium. This was supported

by Mohammad Ziaur Rahman *et al.* [22].

The receiver operating characteristic (ROC) curve processed for the 1 hr post-operative period iPTH assay presented 93.9% sensitivity and 94.4% specificity for a cut of value of  $\leq 14.0$  pg/mL and mean AUC (area under the ROC curve) 0.988. It was statistically significant. The ROC curve processed for the 4 hr postoperative period iPTH assay presented 95.9% sensitivity and 94.4% specificity for a cut of value of  $\leq 09.5$  pg/mL and mean AUC 0.993. It was statistically significant. The ROC curve processed for the 24 hr postoperative period iPTH assay presented 91.8% sensitivity and 94.4% specificity for a cut-off value of  $\leq 11.0$  pg/mL and mean AUC 0.993. It was statistically significant (**Figure 2**).

Chang *et al.* have assessed the optimal time for intact parathyroid hormone (iPTH) measurement for early detection of post-total thyroidectomy (TT) hypocalcemia. A total of 143 patients who underwent total thyroidectomy were included in their single-centre prospective cohort study. iPTH was measured at 10 min and 1, 4, 12, and 24 h postoperatively. When comparing the AUC at each time point, postoperative iPTH at 4 and 12 h showed good predictability (AUC values  $> 0.8$ ) with 100% sensitivity and negative predictive value. In the case of postoperative iPTH at 4 h, sensitivity, specificity, and value were 100.0% and 57.8%, respectively. Sensitivity, specificity, and value for postoperative iPTH at 12 h were 100% and 65.8%, respectively. They suggested that postoperative iPTH could reliably predict hypocalcemia after thyroidectomy, and postoperative iPTH at 4 hr and 12 hr showed good sensitivity and specificity [14]. Our study also gets values very close to them.

Among the various time points, the mean AUC value on the curve at 4 hr postoperative period iPTH assay showed the closest to 1.00 with more sensitivity and specificity for a cut of the value of  $\leq 09.5$  pg/mL.

## 5. Conclusions

The serum iPTH level measurement after a total thyroidectomy can effectively identify patients at risk of developing hypocalcemia. This enables the prompt administration of calcium supplements, rather than waiting for symptoms to appear, and supports the possibility of early discharge. The measurement of serum iPTH level within 1 hr, 4 hrs, and 24 hrs after total thyroidectomy has good sensitivity and specificity. Among them, 4 hr iPTH showed more sensitivity and specificity for a cut of value near the laboratory reference range.

Although optimal care had been tried by the researcher in every step of the study, there were some limitations. It was a center study and purposive sampling was done. We recommend involving multiple centers in randomized clinical trial study to overcome the limitations of this study.

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## Conflicts of Interest

All authors declare no conflict of interest.

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