# The Role of Peri-Operative Parathyroid Hormone Level Measurement after Total or Subtotal Thyroidectomy as a Predictor of Transient and Permanent Hypocalcaemia: A Prospective Study

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## Abstract

**Background:** Thyroid surgery has evolved greatly, from a dangerous surgery to a safe operation with few major risks, small incisions, and favorable outcomes in expert hands. Hypocalcaemia as a result of hypoparathyroidism is the most common complication of thyroidectomy. **Objective:** The aim of the present study was to find out if the degree of early reduction of parathyroid hormone after thyroidectomy can predict the duration of hypocalcaemia. **Patients and methods:** This is a prospective study of new consecutive patients receiving thyroidectomy and preoperative and postoperative time-serial analysis of total calcium, and PTH levels. A total of 40 patients undergoing subtotal thyroidectomy or total thyroidectomy were enrolled in the study. All patients had normal renal function and albumin at the time of surgery. Patient information regarding age, sex, pathology, operative procedure and presence of symptoms of hypocalcemia were recorded. **Results:** There was a statistically significant difference between hypocalcemic and normocalcemic according to total calcium from after 48 h and after 3 m**.** The decreased calcium levels slowly increased and recovered near-completely at 3 m after surgery in both groups. Serum PTH concentrations in the hypocalcemic group dropped in most patients less than 10 min and after 48 and then recovered near to the preoperative level at 3 month after surgery after total thyroidectomy in all patients of hypocacaemic groups. **Conclusion:** The management of patients after total thyroidectomy focuses on close observation for the uncommon event of postoperative hemorrhage and monitoring for hypocalcaemia which results from impaired parathyroid gland function. When the PTH value fell below 23 ng/ml after 10 minutes from thyroidectomy, there was an extremely high likelihood of developing hypocalcemia, and supplementation could have been started earlier for safe, cost effective and early discharge from hospital.

**Keywords:** Parathyroid Hormone Level; Thyroidectomy; Hypocalcaemia

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## INTRODUCTION

Hypocalcaemia is the most common complication of thyroidectomy and a variety of strategies for diagnosing and managing post-thyroidectomy hypocalcaemia have been advocated. Increasingly, the use of intact parathyroid hormone has been utilized to try to predict those patients at risk of developing post-thyroidectomy hypocalcaemia. Intraoperative parathyroid hormone assay has been suggested to have value in predicting the development of postoperative hypo-parathyroidism and hypocalcaemia after thyroid surgery **(1).**

Intraoperative parathyroid hormone has been validated in identification of patients at risk of postoperative hypocalcemia requiring early onset of calcium supplementation therapy and in improving selection of patients eligible for a safe early discharge **(1).**

Post-thyroidectomy parathyroid hormone levels accurately predict hypocalcaemia but lack 100% accuracy. Progressive and severe hypocalcemia is unlikely in the setting of a normal parathyroid hormone level and hence parathyoid hormone can be cautiously used to facilitate discharge within 24 h for many patients. In addition, parathroid hormone levels can be used to implement early treatment with calcium and/or vitamin D supplements to reduce the incidence and severity of hypocalcemia. A single parathyroid hormone measurement taken any time from 10 min to several hours postoperative will provide equally accurate results for predicting post-thyroidectomy hypocalcemia. Routine use of oral calcium supplements may reduce the incidence and severity of post-thyroidectomy hypocalcemia **(2).**

The high incidence of postoperative hypoparathyroidism after total thyroidectomy and the significant morbidity associated with it can account for the sustained efforts to find reliable, affordable markers for the prognosis of this condition. Therefore, a lot of attention has been paid recently to the perioperative measurement of the parathyroid hormone as an immediate indicator showing the parathyroid glands functional status **(3)**. There are a lot of studies in the relevant literature demonstrating that parathyroid hormone is a highly sensitive marker, with high specificity to predict development of postoperative hypocalcaemia. Recent studies analyze in-depth not only the absolute values of parathyroid hormone, but also the dynamics of its levels during surgery. The number and timing of sampling for testing is a matter of discussion. Importance is attached also to the hormone testing methods. Research results determine intraoperative parathyroid hormone as a valuable additional test for early risk assessment of hypocalcaemia allowing prevention and timely treatment of patients at risk **(4).**

Therefore, this study aimed to find out if the degree of early reduction of parathyroid hormone after thyroidectomy can predict the duration of hypocalcaemia.

## PATIENTS AND METHODS

This is a prospective study of new consecutive patients receiving thyroidectomy and preoperative and postoperative time-serial analysis of total calcium, and PTH levels from May 2016 to Aug 2017 in Maadi Military Hospital. All patients had no history of thyroid or neck surgery.

Three Patients diagnosed with papillary thyroid cancer, two patients with follicular thyroid cancer, 15 patients with benign multinodular goiter, 3 patients with recurrent goiter and 8 patients with graves'disease underwent total thyroidectomy and 8 patients with single thyroid nodules who underwent subtotal thyroidectomy. Patients undergoing subtotal thyroidectomy or total thyroidectomy were enrolled in the study.

All patients had normal renal function and albumin at the time of surgery. Patient information regarding age, sex, pathology, operative procedure and presence of symptoms of hypocalcemia were recorded. Informed consent was obtained from all patients.

### Measurement of serum calcium and parathyroid hormone levels.

A preoperative blood sample was drawn the day before surgery for baseline measurement of serum total calcium and PTH levels. Postoperatively time-serial serum concentration of Ca levels was obtained on the day before surgery, at 10 min, 2 days, 3 mon, 6 mon, 9 mon and one year after surgery (reference ranges of serum Ca is 8.5 to 10.5 mg/dl).

Serum intact PTH level were measured with a standard enzyme-linked immunosorbent assay (ELISA) on the day before surgery 10 min, 2 days, 3 mon, 6 mon, 9 mon and one year after surgery after surgery. Expected values from normal adults are 15 to 65 pg/ml. Calcium levels were plotted as a function of time. The difference between the first 2 calcium levels after surgery (10 min and 2 days) was calculated as the percentage change in calcium. In addition, the slope between preoperative and postoperative values of PTH assays was calculated as the percentage change. Postoperative hypocalcemia and follow-up measurement of tests. All patients were clinically evaluated for signs and symptoms of hypocalcemia.

Significant hypocalcemia was defined as a symptomatic patient or Ca level of less than 8.5mg/dl during the hospital stay or at any time after discharge from the hospital. Patients who developed hypocalcemia were started on oral calcium 500–1,500-mg calcium tablets daily and calcitriol 0.25 mcg twice daily was added if the 1,500-mg calcium tablets alone failed to maintain normocalcemia. Intravenous calcium gluconate was administered for significant symptoms. The study protocol required hospitalization of all patients for a minimum of 3 days after surgery for determination of blood tests.

Total thyroidectomy was performed in 32 patients. Hypocalcemia was present in 8 cases (25%). Patients undergoing hemithyroidectomy (n = 8) were considered control subjects not developing hypocalcemia. PTH was measured before surgery and10 minutes after resection of the gland using a rapid (15 minutes) chemiluminescent immunometric assay.

**I- Preoperative assessment:**

**A) Clinically**

**1- Detailed history:** including any history suggestive of hypocalcemia. All of the patients had no history of prior thyroid or neck surgery. All patients had normal renal function and albumin blood levels at the time of surgery. None of the patients had signs indicating metabolic bone disease, and none of the patients were on medications, as oral calcium/vitamin D supplementation, thiazide type diuretics, or antiepileptic agents, known to affect serum calcium metabolism.

**2- Physical examination:** including the body built, weight, pulse and blood pressure, and manifestations suggestive of distant metastases. Inspection, palpation, percussion and auscultation with the aim to determine the following which thyroid lobe is involved, size of the thyroid gland and its consistency, mobility or fixation to the surrounding structures, presence of palpable thrill or audible bruit, and presence of retrosternal extension.

**B) Indirect laryngoscopy:** was done to assess the mobility of the vocal cords.

**C) Radiological assessment:** including chest x-ray posteranterior view, neck ultrasound, and thyroid scan.

**D) Laboratory assessment:** blood samples were collected using conventional venipuncture for Free T3, T4, TSH, Total and ionized serum calcium; and PTH assay.

**Patients included in this study has been divided into two groups:**

Group I: Included patients underwent total thyroidectomy.

Group II: Included patients underwent subtotal thyroidectomy.

**Ethical Consideration:**

An approval of the study was obtained from Cairo University Academic and Ethical Committee. Written informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**II- Operative technique**

Under general endotracheal anesthesia, the patient was placed in a supine position with the neck extended. A low collar incision was made and carried down through the subcutaneous tissue and platysma muscle. Superior subplatysmal flap was developed, and the strap muscles were divided vertically in the midline and retracted laterally and dissected from the relevant thyroid lobe. The middle thyroid vein was ligated.

The superior pole of the thyroid was dissected free, and care was taken to identify and preserve the external branch of the superior laryngeal nerve. The superior pole vessels were ligated very close to the upper pole of the thyroid lobe. The inferior thyroid artery and recurrent laryngeal nerve were identified to preserve blood supply to the parathyroid glands, the inferior thyroid artery was not ligated laterally as a single trunk; rather, its branches were ligated individually on the capsule of the lobe after they have supplied the parathyroid glands. The parathyroid glands were identified, and an attempt was made to leave each with an adequate blood supply while moving the gland off the thyroid lobe. The nerve was gently unroofed from surrounding tissue. The nerve is in greatest danger near the junction of the trachea with the larynx at the ligament of Berry where it is adjacent to the thyroid gland. Once the nerve and parathyroid glands have been identified and preserved, the thyroid lobe was then removed from its tracheal attachments by dividing the ligament of Berry. The contralateral thyroid lobe was removed in a similar manner.

A small suction drain was inserted through a small stab wound; it was generally removed within 24 hours. The strap muscles sutured transversely. Platysma was closed by interrupted sutures and the skin edges were approximated with a running subcuticular 5-0 absorbable suture. Sterile paper tapes (Steri-strips) were then applied and left in place for about a week.

**Postoperative Management:**

During the postoperative period the patients were assessed carefully for the clinical symptoms and signs of hypocalcaemia (fatigue, weakness, numbness around the lips or the tips of the extremities and positive Chvostek’s or Trousseau’s signs were considered to be compatible with mild hypocalcaemia while the carpopedal spasm, convulsions and laryngospasm were considered to be associated with advanced hypocalcaemia).

Patients who developed symptoms and signs of hypocalcaemia were treated by IV calcium gluconate infusion till improvement of symptoms followed by oral calcium and oral active vitamin D till disappearance of symptoms.

Post-operative samples was obtained just on skin closure. After the samples were allowed to clot, serum was separated in aliquots. Serum samples were stored at -20°C till the time of assay. Serum calcium was measured with an automated colorimetric method (Normal value is 1.25-1.35 mg/dl). Serum level of PTH was measured by two-site chemiluminescent enzyme-labeled immunometric assay (Normal value is 15-65 pg/ml).

**Statistical analysis:**

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean. Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance, one-way analysis of variance (ANOVA), and Post Hoc test were used. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value $\leq$0.05 was considered significant, P-value $\leq$0.001 was considered as highly significant, and P-value >0.05 was considered insignificant.

## RESULTS

A total of 40 patients (28 women and 12 men) underwent thyroidectomy over the study period; patient age ranged from 29 to 61 years with a median age of 45 years and mean age of 46.08±7.63 years. The total thyroidectomy (80%) and subtotal thyroidectomy (20%) of type of surgery **(Table 1).**

The indications for operation included 3 patients with papillary thyroid cancer, two patients with follicular thyroid cancer 15 patients with benign multinodular goiter, 3 patients with recurrent goiter and 8 patients with graves' disease underwent total thyroidectomy and 8 patients with single thyroid nodules who underwent subtotal thyroidectomy **(Figure 1)**.

The Benign multi nodullar goiter (40%), Follicular thyroid carcinoma (5%), Papillary thyroid carcinoma (7.5%), Recurrent colloid multinodular goiter (7.5%), Solitary thyroid nodule (20%) and toxic goiter (20%) of etiology of thyroidectomy **(Table 2).** The normocalcemic and hypocalcemic groups had statistical differences of the incidence according to different pathologies (benign vs malignant) and operative procedures (total thyroidectomy vs subtotal thyroidectomy. Serum calcium levels continued to decrease to 2 days after surgery in the hypocalcemic group, but not in the normocalcemic group **(Table 3).**

There was a statistically significant difference between hypocalcemic and normocalcemic according to total calcium from after 48 h and after 3 m **(Table 4).** The decreased calcium levels slowly increased and recovered near-completely at approximately 3 months after surgery in both groups. However, the recovery rate of serum calcium levels was significantly lower in the hypocalcemic group than in the normocalcemic group. All patients with hypocalcemia showed a higher decline after surgery compared with the normocalcemic group **(Figure 2)**.

There was a statistically significant difference between hypocalcemic and normocalcemic according to total calcium from after 48h and after 3m **(Table 5).**

Serum PTH concentrations in the hypocalcemic group dropped in most patients as rapidly as lees than 10 min (rapid PTH assay) and after 48 and then recovered near to the preoperative level at 3 month after surgery after total thyroidectomy in all patients of hypocacaemic groups **(Figure 3)**.

**Table (1): Demographic data of the studied patients**

| Demographic Data | No. | % |
|---|---|---|
| **Gender** | | |
| **Female** | **28** | **70** |
| **Male** | **12** | **30** |
| **Total** | **40** | **100** |
| **Age (years)** | | |
| **Range** | **29-61** | |
| **Mean±SD** | **46.08±7.63** | |

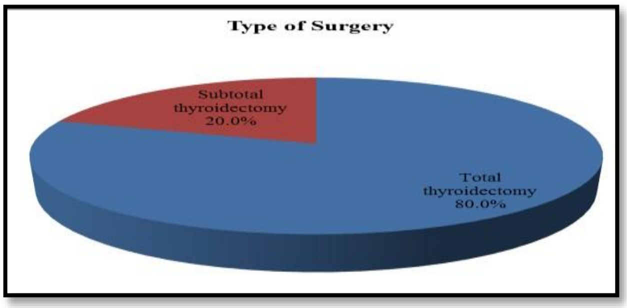


**Figure (1): Type of surgery distribution of the study group.**

**Table (2): Etiology of thyroidectomy distribution of the study group.**

| Etiology of Thyroidectomy | No. | % |
|---|---|---|
| Benign multi nodullar goiter | 16 | 40 |
| Follicular thyroid carcinoma | 2 | 5 |
| Papillary thyroid carcinoma | 3 | 7.5 |
| Recurrent colloid multinodular goiter | 3 | 7.5 |
| Solitary thyroid nodule | 8 | 20 |
| Toxic goiter | 8 | 20 |
| Total | 40 | 100 |

**Table (3): PTH and total calcium descriptive of the study group.**

| | Range | Mean±SD |
|---|---|---|
| **Pre-Operative** | | |
| *PTH (pg/ml)* | 39-56 | 48.50±4.52 |
| *Total Calcium (mg/dL)* | 8.7-10.4 | 9.54±0.49 |
| **10 min after thyroidectomy** | | |
| *PTH (pg/ml)* | 18-55 | 40.15±10.61 |
| *Total Calcium (mg/dL)* | 8.5-10.2 | 9.32±0.46 |
| **48 hrs. After surgery** | | |
| *PTH (pg/ml)* | 7-52 | 35.35±15.16 |
| *Total Calcium (mg/dL)* | 6.1-10 | 8.52±0.97 |
| **3 months After surgery** | | |
| *PTH (pg/ml)* | 23-56 | 44.13±7.12 |
| *Total Calcium (mg/dL)* | 8.4-10.3 | 9.18±0.54 |
| **6 months After surgery** | | |
| *PTH (pg/ml)* | 38-56 | 47.53±4.44 |
| *Total Calcium (mg/dL)* | 8.6-10.2 | 9.37±0.49 |
| **9 months After surgery** | | |
| *PTH (pg/ml)* | 39-56 | 48.05±4.38 |
| *Total Calcium (mg/dL)* | 8.6-10.3 | 9.42±0.52 |
| **1 year After surgery** | | |
| *PTH (pg/ml)* | 38-55 | 47.90±4.07 |
| *Total Calcium (mg/dL)* | 8.7-10.2 | 9.42±0.49 |

*Data were expressed as mean±standard deviation (SD)*

**Table (4): Comparison between patients with and without hypocalcemia according to total calcium (mg/dL).**

| Total Calcium (mg/dL) | Hypocalcemic (N=8) | Normocalcemic (N=32) | t-test | p-value |
|---|---|---|---|---|
| Pre-Operative | 9.38±0.32 | 9.58±0.52 | 1.081 | 0.305 |
| After 10min | 9.20±0.35 | 9.35±0.49 | 0.689 | 0.412 |
| After 48h | 6.76±0.38 | 8.96±0.40 | 197.072 | <0.001 |
| After 3m | 8.65±0.21 | 9.32±0.52 | 12.439 | <0.001 |
| After 6m | 9.18±0.33 | 9.41±0.52 | 1.519 | 0.225 |
| After 9m | 9.16±0.35 | 9.48±0.54 | 2.469 | 0.124 |
| After 1y | 9.25±0.35 | 9.46±0.51 | 1.188 | 0.283 |

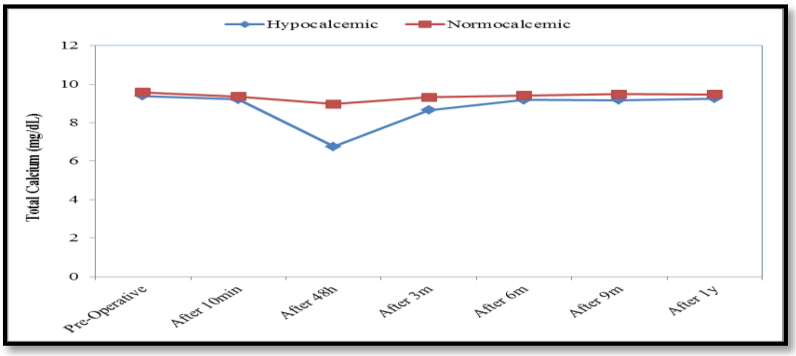


**Figure (2):Comparison between patients with and without hypocalcemia according to total calcium (mg/dL).**

**Table (5):Comparison between patients with and without hypocalcemia according to total calcium (mg/dL).**

| Total Calcium (mg/dL) | Hypocalcemic (N=8) | Normocalcemic (N=32) | t-test | p-value |
|---|---|---|---|---|
| **Pre-Operative** | **9.38±0.32** | **9.58±0.52** | **1.081** | **0.305** |
| **After 10min** | **9.20±0.35** | **9.35±0.49** | **0.689** | **0.412** |
| **After 48h** | **6.76±0.38** | **8.96±0.40** | **197.072** | **<0.001** |
| **After 3m** | **8.65±0.21** | **9.32±0.52** | **12.439** | **<0.001** |
| **After 6m** | **9.18±0.33** | **9.41±0.52** | **1.519** | **0.225** |
| **After 9m** | **9.16±0.35** | **9.48±0.54** | **2.469** | **0.124** |
| **After 1y** | **9.25±0.35** | **9.46±0.51** | **1.188** | **0.283** |

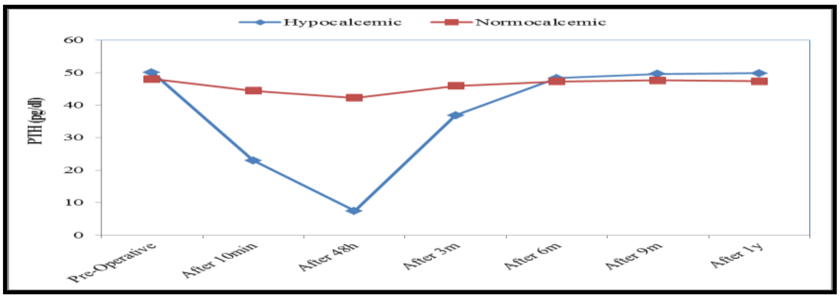


**Figure (3):Comparison between patients with and without hypocalcemia according PTH.**

There was a statistically significant difference between hypocalcemic and normocalcemic according to PTH from after 10min to after 3m **(Table 6).**Analysis of the test cutoff values indicated much higher sensitivity for the PTH levels at 10 minutes and decline percentages after thyroidectomy **(Table 7)**. The sensitivity of serum calcium levels after surgery at the cutoff point increased slightly at 48 hours (100%) compared with those obtained at 10 min after thyroidectomy (88%). Receiver operating characteristics (ROC) curve was used to define the best cut off value of Total Calcium (mg/ml) as the following: pre-operative which was <9.5, with accuracy 58% ; 10 min after thyroidectomy <9.3, with accuracy 59%; 48 hrs after surgery <7.2, with accuracy 100%; 3 months after surgery <8.7, with accuracy 91% ; 6 months after surgery <9.3, with accuracy 62%; 9 months after surgery <9.2, with accuracy 66%; and 1 years after surgery <9.2, with accuracy 57% **(Figure 4)**.

About the sensitivity and specificity of PTH levels an algorithm was developed for patients undergoing total thyroidectomy. We made criteria based on the preoperative and intraoperative rapid PTH assays and postoperative PTH levels **(Table 8)**. ROC curve was used to define the best cut off value of PTH as the following: pre-operative which was >48, with accuracy 66.4%; 10 min after thyroidectomy <23, with accuracy 96% ; 48 hrs after surgery <9, with accuracy 100%; 3 months after surgery <40, with accuracy 76% ; 6 months after surgery >46, with accuracy 62%; 9 months after surgery >46, with accuracy 65%; and 1 years after surgery >47, with accuracy 70% **(Figure 5)**.

**Table (6): Comparison between patients with and without hypocalcemia according PTH.**

| PTH (pg/ml) | Hypocalcemic (N=8) | Normocalcemic (N=32) | t-test | p-value |
|---|---|---|---|---|
| Pre-Operative | 50.13±1.36 | 48.09±4.95 | 1.300 | 0.261 |
| After 10min | 23.00±7.46 | 44.44±5.85 | 76.981 | <0.001 |
| After 48h | 7.50±0.76 | 42.31±6.22 | 245.027 | <0.001 |
| After 3m | 36.88±9.25 | 45.94±5.25 | 13.749 | <0.001 |
| After 6m | 48.38±2.50 | 47.31±4.82 | 0.360 | 0.552 |
| After 9m | 49.63±1.77 | 47.66±4.76 | 1.304 | 0.261 |
| After 1y | 49.88±1.36 | 47.41±4.38 | 2.436 | 0.127 |

**Table (7): Accuracy of the cutoff values in predicting postoperative in Total Calcium (mg/ml) hypocalcemia.**

| | Cut-off | Sen. | Sp. | PPV (positive predictive value) | NPV (negative predictive value) | Accuracy |
|---|---|---|---|---|---|---|
| Pre-Operative total calcium (pg/ml) | <9.5 | 88% | 53% | 31% | 94% | 58% |
| 10min after thyroidectomy | <9.3 | 88% | 47% | 29% | 94% | 59% |
| 48 hrs. After surgery | <7.2 | 100% | 100% | 100% | 100% | 100% |
| 3 months after surgery | <8.7 | 75% | 88% | 60% | 93% | 91% |
| 6 months after surgery | <9.3 | 88% | 50% | 30% | 94% | 62% |
| 9 months after surgery | <9.2 | 87% | 63% | 37% | 95% | 66% |
| 1 years after surgery | <9.2 | 88% | 56% | 33% | 95% | 57% |

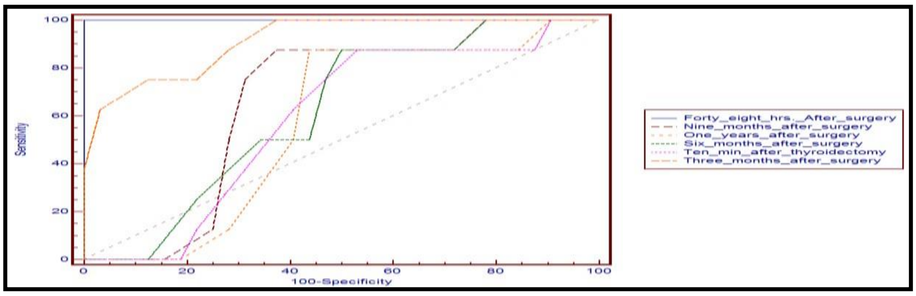


**Figure (4): Receiver-operating characteristic (ROC) curve for prediction of predicting postoperative in Total Calcium (mg/ml) hypocalcemia.**

**Table (8): Accuracy of the cutoff values in predicting postoperative in PTH hypocalcemia.**

| | Cut-off | Sen. | Spe. | PPV (positive predictive value) | NPV (negative predictive value) | Accuracy |
|---|---|---|---|---|---|---|
| Pre-Operative PTH (pg/ml) | >48 | 100% | 59% | 38% | 100% | 66.4% |
| 10min after thyroidectomy | <23 | 88% | 100% | 100% | 97% | 96% |
| 48 hrs. After surgery | <9 | 100% | 100% | 100% | 100% | 100% |
| 3 months after surgery | <40 | 50% | 94% | 67% | 88% | 76% |

| | | | | | | |
|---|---|---|---|---|---|---|
| **6 months after surgery** | **>46** | **88%** | **56%** | **33%** | **95%** | **62%** |
| **9 months after surgery** | **>46** | **100%** | **53%** | **35%** | **100%** | **65%** |
| **1 years after surgery** | **>47** | **100%** | **59%** | **38%** | **100%** | **70%** |

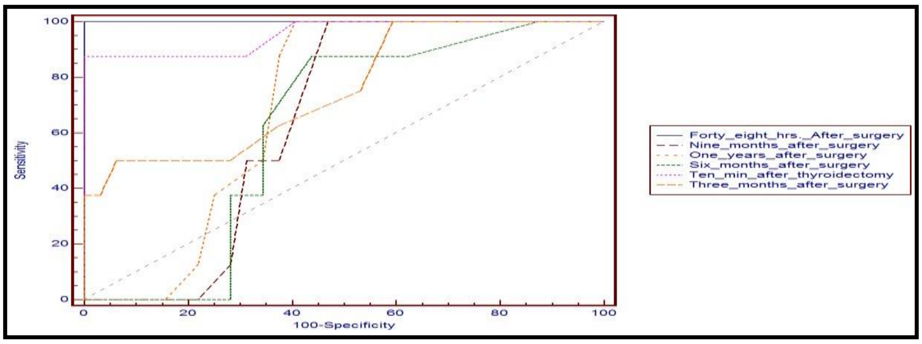


**Figure (5): Receiver-operating characteristic (ROC) curve for prediction of predicting postoperative in PTH hypocalcemia.**

## DISCUSSION:

Thyroidectomy can cause hypoparathyroidism from removal of parathyroid glands or damage to their blood supply. This is the most frequent postoperative complication, and the subsequent onset of hypocalcemia can pose severe problems **(5).**

Post-thyroidectomy hypocalcemia is a major contributing factor in delayed hospital discharge and dissuading surgeons from ambulatory thyroidectomy. In addition, because potentially life threatening hypocalcemia may not develop until 24–48 h after surgery besides postoperative bleeding and hematoma formation, hypoparathyroidism is a major reason for delayed hospital discharge **(6).**

Postoperative transient hypoparathyroidism leading to hypocalcemia is the one of the most frequent morbidities following total thyroidectomy, with incidence ranging between 3 and 40 % **Lang et al. (6)** in comparison to our study with incidence of Postoperative transient hypoparathyroidism about 40 %.

Although the development of hypocalcemia is multifactorial, clinically significant hypocalcemia after thyroid surgery occur secondary to impairment of parathyroid function in most cases. Postoperative hypocalcemia is usually transient, and the incidence of permanent hypoparathyroidism is 2% or less in most surgical units with experience in total thyroidectomy **Roh et al. (7)**. In comparison to our study, 8 cases out of 40 manifested transient hypocalcaemia with no detected cases of permanent hypocalcaemia.

Although it is self-limiting in most patients, postoperative hypocalcemia is of particular concern because of a delay in the manifestation and a consequent prolonged hospitalization or readmission. Therefore, efforts have been made to predict which patients are susceptible to the development of this complication and will require supplementation of oral calcium and/or vitamin D **(7).** Because of a search for earlier predictors, the short half-life of PTH has led to increased interest in intraoperative PTH monitoring as an early marker of hypocalcemia **(5).**

Given that patients who undergo this kind of surgery are usually discharged early (most often the day after surgery, unless complications occur) reliable markers allowing early diagnosis of hypocalcemia have been thoroughly sought **(5).**

To safely manage postoperative hypoparathyroidism hypocalcemia, three approaches had been described, namely, serial calcium (Ca) monitoring, routine Ca supplementation, and parathyroid hormone (PTH)-directed supplementation. Serial Ca monitoring is often adopted because Ca testing is widely available but involves patients staying for at least 1–2 nights in hospital. In the era of cost containment, there has been a gradual shift from serial Ca monitoring to the other two approaches **(6).**

Close monitoring of early serum calcium levels is commonly used to identify postoperative hypocalcemia. However, multiple blood samplings to at least the morning after surgery need to be done and early prediction of postoperative hypocalcemia within the same day of operation is impossible. Because serum parathyroid hormone (PTH) is known to be a more useful predictor of impending postoperative hypocalcemia, rapid PTH assay has been used to measure intraoperative PTH levels **(7).**

The aim of our study was to assess perioperative PTH measures as very early predictors of hypocalcemia after treatment to attempt making this kind of surgery an ambulatory procedure in our hospital so that patients can be discharged the day of surgery provided that no other risks exist.

For **Alía et al. (5)** study patients undergoing hemithyroidectomy as control subjects because they do not have hypocalcemia secondary to hypoparathyroidism. They seemed to show just the transient biochemical hypocalcemia already reported after many surgeries**.** In our study, all patients undergoing hemithyroidectomy not manifested by hypocalcaemia or hypoparathyroidism subsequently considered as control subjects.

Early attempts at identifying patients at risk of hypocalcemia primarily attempted to use the change in sequential calcium over time and calculate slope to predict risk of hypocalcemia. The main concern with this technique is that parathyroid hormone levels had to be drawn over an 8 hour period to be predictive, and there was no correlation seen with early calcium levels, thus limiting the utility of calcium slopes in facilitating early discharge from hospital **(8).**

In our study, 10 to 15 minutes parathyroid hormone measurement after thyroidectomy can be used as a predictor of hypocalcaemia with accuracy 96%, thus limiting unnecessary calcium supplementation and facilitate early hospital discharge.

In **Lang et al. (6)** analysis, test sensitivity and specificity of parathyroid hormone on skin closure were 82.4 and 95.0 %, respectively**.** For our study with parathyroid hormone 10 to 15 minutes after thyroidectomy with sensitivity 88% and specificity 100%.

However, we assure that our study results can strengthen the applicability of rapid ioPTH assay in thyroid surgery and suggest a guide that can contribute to managing postthyroidectomy patients. Another merit of this study is a prospective time-serial observation of serum calcium and PTH levels up to one year in comparison to **Roh et al. (9)** who conducted 6 months after surgery.

In **Lang et al. (6)** clinical setting, a single quick PTH level measurement taken at the time of skin closure (PTH-SC) while the patient is still anesthetized would be preferred because no extra pain is inflicted while drawing blood and the PTH result would be available sooner to facilitate ambulatory surgery.

We evaluated prospectively the accuracy and reliability of quick PTH-SC in predicting clinically relevant postoperative hypocalcemia. Therefore, PTH-SC might not only be more accurate and reliable in predicting clinically relevant hypocalcemia than serial Ca monitoring, it might also eliminate the need for drawing blood multiple times and an overnight stay.

In our analysis, test sensitivity and specificity of PTH-SC were 88 and 100 % respectively. In comparison to **Lang et al. (6)** characteristic curve (AUC) between serum Ca slopes, preoperative adjusted Ca, PTH-SC, PTH-D1, and a combined preoperative Ca and PTH-SC score. In predicting hypocalcemia, the best cutoff values for PTH-SC and PTH-D1 were 1.0 pmol/L**.**

The results of **Noordzij et al. (10)** study demonstrated and confirmed the usefulness of the PTH assay in thyroid surgery. A single PTH threshold (65% decrease compared with a preoperative level) checked 6 hours after completing thyroidectomy has a sensitivity of 96.4% and specificity of 91.4% in detecting postoperative hypocalcemia**.**

Patients with a less than 65% decline in 6-hour postoperative PTH have a low risk of hypocalcemia and could be discharged after appropriate observation for other complications such as a hematoma.

If the surgeon desires to lessen the risk of sending home a patient who would subsequently become hypocalcemic or avoid unnecessarily treating a patient who is not going to become hypocalcemic, a two cut-off approach could be used. For example, using the 1- to 2-hour postoperative values from, cut-offs of 50% and 90% could be used. Additionally, only patients with a 90% decrease of PTH would be treated with calcium supplementation on the day of surgery. Using these two cut-offs, the sensitivity and specificity would be greater than if a single cut-off was used. The down side to this approach is that patients in the middle (with a PTH decrease between 50% and 90%) would not be acted on early. These patients would require traditional calcium monitoring until their serum calcium leveled off **(10).**

For our study, cut off value of parathyroid hormone 23 ng/dl can be used as a value to allow for early discharge after appropriate observation for other complications. So, for patients with less than 49 % decrease of parathyroid hormone have a low risk of hypocalcemia and could be discharged after appropriate observation for other complications. These patients should still be educated about symptoms of hypocalcemia and instructed to return immediately if these occur. Despite the overall excellent accuracy of PTH in predicting hypocalcemia after thyroidectomy, false positives and negatives still occur.

For **Roh et al. (7)** study PTH levels were measured at 1 hour or later after the surgery for more confident prediction of postoperative hypocalcemia in several studies. However, other studies have advocated that ioPTH levels obtained immediately after thyroid dissection could be used reliably to predict postoperative hypocalcemia. In addition, it was suggested that a low ioPTH level (<10 pg/mL) may be indicator of vascular injury of an intact gland and may be a guide to more aggressive assessment of the vascularity in the parathyroid glands, and devascularized glands should be considered for autotransplantation**.**

The vascularity of parathyroid glands can be rechecked based on the ioPTH levels routinely measured at the end of thyroidectomy and evaluated by visual inspection of their vascular pedicles and small incision of the glands to access bleeding. In fact, because the in vivo half-life of PTH is as short as 2 to 5 minutes, a decline in PTH levels can occur within a few minutes after bilateral thyroid dissection. Thus, the ioPTH level obtained immediately after thyroidectomy can be used to predict postoperative hypocalcemia **(7).**

**SywaK et al. (11)** study also showed that the ioPTH levels were significantly correlated with standard PTH levels measured 10 min and 48hours after thyroidectomy. However, there was no significant correlation between ioPTH value and iCa level until the morning after surgery. This may be due to a delay in the decline of serum calcium level (to at least 8 hours after the surgery)**.**

Patients fulfilling criteria were normocalcemic in our study. The cutoff values can be used to determine which patients will be safely discharged early or will need close monitoring.

Our proposed algorithm is very simple, cost effective, and evidence-based. There is no need for additional early calcium monitoring in the algorithm for postoperative patient management. The algorithm helps select which patients undergoing total thyroidectomy can be discharged the same day as the operation. This approach will significantly reduce the total medical cost compared with patients requiring prolonged hospitalization more than 24 hours; this needs to be strengthened by further randomized studies comparing patients who the same day discharge is allowed for or not. This can also be supported prior studies that have already reviewed the cost-effectiveness of rapid PTH assay, resulting from avoidance of prolonged hospitalization and multiple biochemical testing.

According to **Vescan et al. (8)** protocol, most of the patients are suitable for discharge within 23 h of surgery. It is likely that those of the hypocalcaemic group may avoid a lengthier than usual hospitalization because of the timely initiation of treatment. This approach has the potential to streamline length of stay**.**

## CONCLUSION:

Hypocalcemia is the most usual complication after thyroidectomy. Although the reported frequency is variable probably low because the usual practice of administering calcium supplements to all patients to allow for early discharge may mask the real frequency of hypocalcemia.

The management of patients after total thyroidectomy focuses on close observation for the uncommon event of postoperative hemorrhage and monitoring for hypocalcaemia which results from impaired parathyroid gland function. When the PTH value fell below 23 ng/ml after 10 minutes from thyroidectomy, there was an extremely high likelihood of developing hypocalcemia, and supplementation could have been started earlier for safe, cost effective and early discharge from hospital.

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## REFERENCES:

1- **Barczyński, M., Cichoń, S., Konturek, A., & Cichoń, W. (2008)**. Applicability of intraoperative parathyroid hormone assay during total thyroidectomy as a guide for the surgeon to selective parathyroid tissue autotransplantation. *World journal of surgery*, *32*, 822-828.

2- **Lee, D. R., Hinson, A. M., Siegel, E. R., Steelman, S. C., Stack Jr, B. C. (2015).** Comparison of intraoperative versus postoperative parathyroid hormone levels to predict hypocalcemia earlier after total thyroidectomy. *Otolaryngology–Head and Neck Surgery*, *153*(3), 343-349.

3- **Barczyński, M., Cichoń, S., & Konturek, A. (2007).** Which criterion of intraoperative iPTH assay is the most accurate in prediction of true serum calcium levels after thyroid surgery?. *Langenbeck's archives of surgery*, *392*, 693-698.

4- **Pattou, F., Combemale, F., Fabre, S., Carnaille, B., Decoulx, M., Wemeau, J. L., ... & Proye, C. (1998).** Hypocalcemia following thyroid surgery: incidence and prediction of outcome. *World journal of surgery*, *22*, 718-724.

5- **Alía, P., Moreno, P., Rigo, R., Francos, J. M., & Navarro, M. Á. (2007)**. Postresection parathyroid hormone and parathyroid hormone decline accurately predict hypocalcemia after thyroidectomy. *American journal of clinical pathology*, *127*(4), 592-597.

6- **Lang, B. H. H., Yih, P. C. L., Ng, K. K. (2012)**. A prospective evaluation of quick intraoperative parathyroid hormone assay at the time of skin closure in predicting clinically relevant hypocalcemia after thyroidectomy. *World journal of surgery*, *36*, 1300-1306.

7- **Roh, J. L., Park, C. I. (2006)**. Routine oral calcium and vitamin D supplements for prevention of hypocalcemia after total thyroidectomy. *The American journal of surgery*, *192*(5), 675-678.

8- **Vescan, A., Witterick, I., & Freeman, J. (2005)**. Parathyroid hormone as a predictor of hypocalcemia after thyroidectomy. *The Laryngoscope*, *115*(12), 2105-2108.

9- **Roh, J. L., Kim, J. M., Park, C. I. (2011)**. Central compartment reoperation for recurrent/persistent differentiated thyroid cancer: patterns of recurrence, morbidity, and prediction of postoperative hypocalcemia. *Annals of surgical oncology*, *18*, 1312-1318.

10- **Noordzij, J. P., Lee, S. L., Bernet, V. J., Payne, R. J., Dietrich, M. S. (2007)**. Early prediction of hypocalcemia after thyroidectomy using parathyroid hormone: an analysis of pooled individual patient data from nine observational studies. *Journal of the American College of Surgeons*, *205*(6), 748-754.

11- **Sywak, M. S., Palazzo, F. F., Sidhu, S. B., & Delbridge, L. W. (2007)**. Parathyroid hormone assay predicts hypocalcaemia after total thyroidectomy. *ANZ journal of surgery*, *77*(8), 667-670.