

Role of Postoperative Intact Parathyroid Hormone Levels in Predicting Hypocalcaemia after Thyroidectomy

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ABSTRACT

Objective: To determine the sensitivity and specificity of intact parathyroid hormone (iPTH) levels in predicting hypocalcaemia after thyroidectomy.

Study Design: A descriptive cross-sectional study.

Place and Duration of the Study: Department of General Surgery, Shifa International Hospital and Shifa Foundation, Islamabad, from May 2021 to 2022.

Methodology: The sample size was calculated to be 205 with consecutive non-probability sampling. Serum iPTH levels and serum calcium levels were measured postoperatively at 6 hours and 24 hours and recorded in a proforma for analysis. After collection, the data were entered and analysed using SPSS version 24.0.

Results: Among 205 patients, 157 (76.6%) were females and 48 (23.4%) were males. At 6 hours postoperatively, 121 (59%) patients had normal iPTH levels and 123 (60%) patients had normal serum calcium levels ($p = 0.15$). At 24-hour, 130 (63.4%) patients had normal iPTH levels and 92 (44.9%) patients had normal serum calcium levels ($p = 0.001$). Overall, 8 (3.9%) patients developed symptomatic hypocalcaemia ($p = <0.001$). The sensitivity and specificity of iPTH levels at ≤ 15 pg/ml were 100% and 70%, respectively, but at 24 pg/ml cut-off level, the specificity increased to 90% with sensitivity of 100%.

Conclusion: Low serum iPTH levels at 6 hours after surgery can predict hypocalcaemia in patients undergoing thyroidectomy, even if serum calcium levels appear normal at that time.

Key Words: Parathyroid hormone, Serum calcium, Hypocalcaemia, Total thyroidectomy, Calcium homeostasis.

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INTRODUCTION

Thyroid gland is one of the important endocrine glands in the human body, and diseases of the thyroid are considered to be the most common endocrine diseases. Most of these diseases are managed by thyroidectomy, either total or subtotal. Hypoparathyroidism and hypocalcaemia are considered the most important complications after total and subtotal thyroidectomy.¹ During surgery, the blood supply to the parathyroid glands gets compromised leading to hypocalcaemia. Hypocalcaemia can be transient or permanent depending upon the degree of damage to the parathyroid glands. Meticulous dissection is performed to preserve all four parathyroid glands but in some cases, where it is not possible, auto-transplantation has been used as well as a preventive measure for hypocalcaemia.²

Parathyroid hormone (PTH) is secreted from the parathyroid glands in response to decreased levels of calcium in the blood. High levels of calcium in the blood, will create a feedback loop and will suppress the release of PTH. After injury to the parathyroid glands, the release of PTH is interrupted, leading to decreased calcium levels in the body.^{3,4} In the literature, PTH levels have been used as a predictor of hypocalcaemia, and serum intact PTH levels of <10 pg/ml are taken as indicators of hypoparathyroidism after total thyroidectomy. This study aimed to determine the sensitivity and specificity of iPTH levels in predicting hypocalcaemia after total or subtotal thyroidectomy at a single centre in Pakistan.

METHODOLOGY

This descriptive cross-sectional study was conducted on the patients admitted for thyroidectomy, at the Shifa International Hospital and Shifa Foundation, Islamabad. Sample size of 205 was calculated using the WHO calculator with non-probability consecutive sampling and in a duration of 12 months from May 2021 to 2022. The confidence interval was kept as 95%, absolute precision at 3.5%, and the anticipated population prevalence at 7%. Patients admitted for total or subtotal thyroidectomy with an age range of 16-60 years, and both genders were included. Patients with chronic kidney disease (CKD), patients already on calcium or vitamin D supplements, head and neck

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malignancies, medullary carcinoma of thyroid on fine needle aspiration cytology (FNAC), and hyperparathyroidism were excluded. Ethical approval was obtained from the Institutional Review Board (IRB) of the Shifa International Hospital, Islamabad. Patients diagnosed with goitre were admitted for surgical management one night before the surgery. After the patients underwent surgery, they were shifted back to an inpatient facility, where serum iPTH and calcium levels were measured firstly at 6 hours postoperatively. iPTH levels were assessed using electrochemiluminescent immunoassay (ECLIA). At this stage, only symptomatic patients with hypocalcaemia were administered calcium gluconate 10%, diluted in 10 ml of normal saline and administered over 10 minutes intravenously. All patients were kept under close observation. Subsequent serum levels of iPTH and calcium were obtained after 24 hours of the procedure. All hypocalcaemia patients received calcium and vitamin D supplementation. Patients' data were collected and documented in proforma.

After collection, it was entered and analysed using the Statistical Package for Social Sciences (SPSS).version 24.0 (IBM Corp, Armonk, NY, USA). Qualitative variables such as, age categories and gender were expressed as frequencies and percentages. Quantitative variables such as age, serum iPTH, and calcium levels were expressed as mean ± standard deviation (SD).

Relationship of iPTH with hypocalcaemia was determined through a 2 × 2 table and Chi-square test considering a significant value of $p < 0.05$. The receiver operating characteristic curve (ROC curve) was used to calculate the sensitivity and specificity of iPTH levels for hypocalcaemia.

RESULTS

In this study, the total number of patients was 205. Among these, females were 157 (76.6%) and males were 48 (23.4%). In age categories, 102 (49.8%) patients belonged to 46-60 years of age. The majority of the patients had normal iPTH levels at 6 hours postoperatively. At 6 hours postoperatively, 123 (60%) patients had normal serum calcium. At 24 hours, 130 (63.4%) patients had normal iPTH and 92 (44.9%) patients had normal serum calcium levels. In total, only 8 (3.9%) patients developed symptomatic hypocalcaemia.

At 6 hours postoperatively, the mean iPTH levels were 24.45 ± 22.05 pg/ml and serum calcium was 8.26 ± 0.68 mg/dl as shown in Table I. The relationship between iPTH levels at 6 hours and serum calcium levels at 24 hours was significant ($p < 0.001$). The relationship between iPTH levels and serum calcium at 24 hours was also significant ($p < 0.001$). The sensitivity and specificity of iPTH levels at ≤ 15 pg/ml were 100% and 70%, respectively, but at 24 pg/ml cut-off level, the specificity increased to 90% with a sensitivity of 100%. The area under the curve (AUC) values for sensitivity and specificity were 58.82% and 47.37%, respectively as shown in Figure 1 and 2.

Table I: Descriptive statistics of serum parathyroid hormone (PTH) levels in pg/ml and serum calcium levels in mg/dl (n = 205).

Serum levels	Minimum	Maximum	Mean	Standard Deviation (SD)
Serum PTH at 6 hours	1.0	94.0	24.45	22.05
Serum calcium levels at 6 hours	3.0	10	8.48	0.81
Serum PTH levels at 24 hours	1.0	78	23.45	19.06
Serum calcium levels at 24 hours	6.2	10.10	8.26	1.92

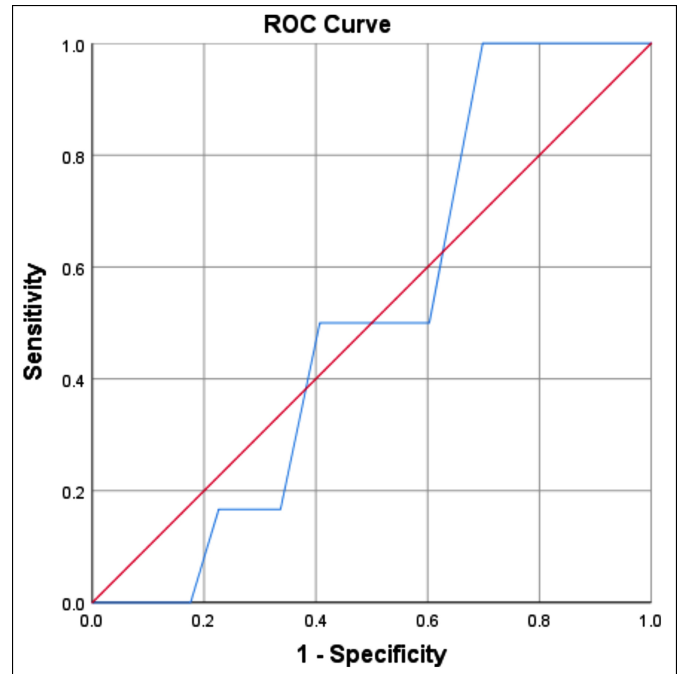


Figure 1: With serum parathyroid hormone cut-off level at 15 pg/ml, sensitivity is 100% and specificity is 70%.

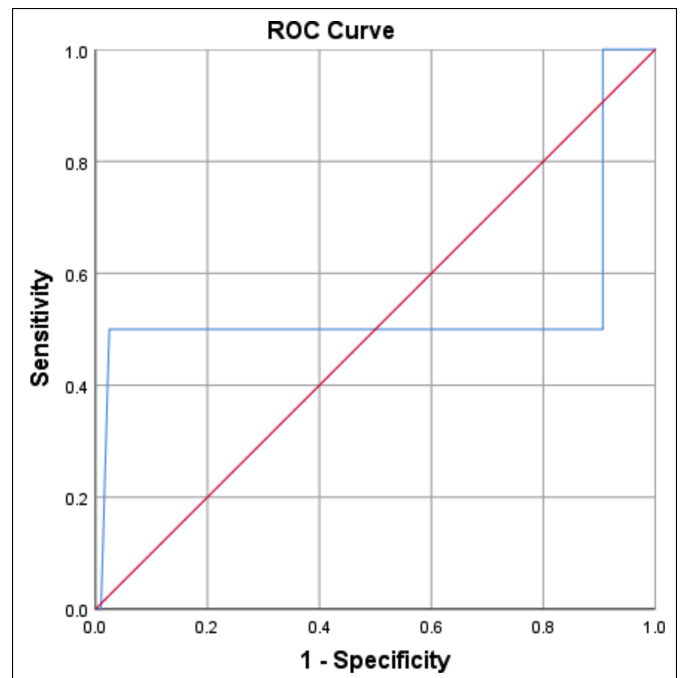


Figure 2: With serum parathyroid hormone cut-off level of ≤ 24 pg/ml, sensitivity is 100% and specificity 90%.

DISCUSSION

Iodine deficiency is considered the most common cause of goitre. Globally, 2.2 billion people are affected by this deficiency.⁵ However, with the fortification of salt with iodine, the prevalence of iodine deficiency dropped from 70 to 50% in the past decade but is still high.⁶ The second most common cause of goitre is Graves' disease. Females are mostly affected by thyroid diseases as reported in international literature as well as from Pakistan.⁷ This study showed the same trend with 76.6% female patients and 23.4% males. However, another study of 392 cases by Khan *et al.* showed no significant difference between gender groups and thyroid profiles.⁸

Hypoparathyroidism is a common complication after total and subtotal thyroidectomy.⁹ Despite careful dissection and proper identification of parathyroid glands, compromise to blood supply is attributed as a major factor for hypoparathyroidism and studies have suggested auto-transplantation of parathyroid glands in case of inadvertent removal of gland for prevention of hypoparathyroidism.² A meta-analysis done by Chen *et al.* for risk factors of hypocalcaemia showed that not only hypoparathyroidism after thyroidectomy is a risk factor but also patients who underwent lymph node dissection were at increased risk for hypocalcaemia.¹⁰

In this study, 41% of the patients developed biochemical hypoparathyroidism. Despite early hypoparathyroidism, only 40% of the patients had low serum calcium levels at 6 hours after thyroidectomy. However, after 24 hours, this percentage increased to 55.1% and serum levels dropped further (6 - 6.5/mg/dl) with a significant p-value of <0.001 between iPTH levels at 6 hours and calcium levels at 24 hours. This shows that an early drop in serum iPTH levels at 6 hours can predict hypocalcaemia. The same findings are reported in a study conducted by Noureldine *et al.* who reported a p-value of <0.001.¹¹

An analysis by Algarni *et al.* of 40 patients undergoing total thyroidectomy for thyroid cancer, showed comparable findings of low PTH and calcium levels at 6 hours postoperatively with p-value of 0.014.¹² However, the current study showed that calcium levels further fall, and by 24 hours after surgery, serum PTH levels at 6 hours become predictive of hypocalcaemia developing at 24 hours after surgery (p <0.001). Suwannasarn *et al.* obtained iPTH and calcium levels at 4 hours postoperatively and found significant p-value of <0.01.¹³

A study performed in India by Cherian *et al.* showed a significant association between serum iPTH levels and serum calcium levels at 4 hours (p = 0.029).¹⁴ However, other studies conducted for iPTH levels' relationship with serum calcium at 4 hours did not show significant outcomes.¹⁵

Although no consensus is found in the literature about the best time for serum iPTH levels, Sahli *et al.*'s study found that PTH levels at 1 hour postoperatively are not predictive for hypocalcaemia. Although the sample size was large in the study (218), all patients were pre-treated with vitamin D and calcium, which could have influenced the results.¹⁶

A study done by Arnepalli *et al.* in India on 43 patients measured PTH levels at 1 hour after surgery and calcium levels at 1, 2, 3, and 4 days after surgery. They found that at an iPTH level of 15 pg/ml, the sensitivity of PTH in predicting hypocalcaemia was 93% and the specificity was 91.6%.¹⁷ The present study showed that the sensitivity of PTH as an early predictor of hypocalcaemia was 100% and specificity was 70% with iPTH levels of ≤15 pg/ml; however, with cut-off levels of ≤24 pg/ml, the sensitivity remained at 100% but the specificity increased to 90%. As found in the study conducted by Galy-Bernadoy *et al.* in France, a difference in sensitivity and specificity was found with two different outcomes and reported better sensitivity and specificity with two threshold values.¹⁸ This study's data and findings support the hypothesis that serum PTH levels at 6 hours after thyroidectomy, if found to be low, can predict hypocalcaemia, although initially, the patient may have normal levels of serum calcium which will eventually drop after 24 hours of thyroidectomy.

In this study, follow-up data are not available for those patients who developed hypocalcaemia and hypoparathyroidism to evaluate if this episode was transient or permanent.

No preoperative serum calcium and iPTH levels were available for comparison of those patients whose calcium levels remained in the normal range postoperatively. Thus, the authors were unable to calculate proper drops in their levels if any, and their significance.

CONCLUSION

Serum iPTH levels at 6 hours after surgery can predict hypocalcaemia in patients undergoing thyroidectomy, even if serum calcium levels appear normal at that time. This study shows that if 6-hour iPTH levels are ≤15 pg/ml, these are 100% specific in predicting hypocalcaemia at 24 hours. Consequently, patients can be managed early and those who do not require treatment can be discharged early without oral calcium and vitamin D supplements.

ETHICAL APPROVAL:

Ethical approval for this study was obtained from Institutional Review Board and Ethical Committee of Shifa International Hospital, Ltd. and Shifa Tameer-e-Millat University (STMU), Islamabad, Pakistan (IRB no. 054-874-2020).

PATIENTS' CONSENT:

All patients provided written informed consent.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

SA: Conception or design of the work and interpretation of the data.

HZA: Conception or design of the work.

SL: Analysis and interpretation of the data.

FF: Drafting the work and critically revising the manuscript for the important intellectual content.

All authors approved the final version of the manuscript to be published.

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