

## Original Research Article

# Parathyroid hormone assay following total thyroidectomy for early prediction of post-operative hypocalcemia

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### ABSTRACT

**Background:** Detecting post-operative hypocalcaemia following total thyroidectomy using serum parathyroid hormone levels would help in an earlier and a definitive treatment plan in treating hypocalcaemia.

**Methods:** This was a prospective interventional study done in a tertiary care teaching hospital. This was mainly done to assess the post-operative hypocalcemia following total thyroidectomy using parathyroid hormone levels and to assess the correlation between the two. With a baseline levels recorded patients underwent a post-operative evaluation of parathyroid hormone 1 hour after total thyroidectomy and serum calcium levels on day 1, 2, 3 and 4 after surgery. The same was statically analyzed to find a correlation between parathyroid hormone levels and the degree of hypocalcemia and evaluated to see if parathyroid hormone was a reliable clinical indicator.

**Results:** A total of 43 patients were included in the study and the parathyroid hormone levels were assessed following surgery, the same was plotted statistically. Sensitivity of parathyroid hormone drop by 75% in predicting hypocalcaemia was 95%. 50% drop in parathyroid hormone levels was a sensitive predictor of hypocalcaemia. A PTH value of less than 15.1pg/ml was highly specific and sensitive indicator of hypocalcaemia.

**Conclusions:** Parathyroid hormone Assay following total thyroidectomy is reliable for early prediction of hypocalcaemia. Patients with a parathyroid hormone level <9pg/ml or with 75% drop in parathyroid hormone level are at a high risk for hypocalcaemia and would require calcium supplementation.

**Keywords:** Hypocalcaemia, Parathyroid hormone assay, Total thyroidectomy

### INTRODUCTION

Incidence of post-operative hypocalcaemia following total thyroidectomies can be taken as factor for assessing the quality of the surgery performed. Development of hypocalcaemia is likely to be multifactorial, common causes being devascularisation, secondary to parathyroid injury, inadvertent removal of parathyroid gland, haemodilution and “stunning” from dissection.<sup>1</sup>

Post-operative hypocalcaemia occurs 24-48 hours after total thyroidectomy and may be delayed up to post-operative day 4 which in turn increases the hospital stay.

Therefore, detecting patients requiring calcium replacement therapy with serial calcium measurements can take multiple blood tests over several days. Placing all patients on calcium therapy unnecessarily commits many patients to unnecessary treatment and puts them at risk for hypercalcaemia.

A clinical laboratory method for early prediction of postoperative hypocalcaemia could, therefore, facilitate earlier implementation of treatment, and early discharge.

Aims and objectives of the study were to evaluate the accuracy of post-operative parathyroid hormone level in

predicting hypocalcaemia following total thyroidectomy and to assess correlation between absolute parathyroid hormone level with post-operative hypocalcaemia. To find the cut-off value of post-operative parathyroid hormone level which can predict hypocalcaemia and to assess the correlation between parathyroid hormone decline and post-operative hypocalcaemia.

**METHODS**

The study was a prospective interventional study conducted under the department of general surgery, Kasturba Hospital, Manipal between October 2015 to August 2017. Forty-eight patients who underwent total thyroidectomy over a period of one year and 10 months were studied. Each patient was included only once in the study. All the patients included in the study were informed about the objectives and nature of the study.

**Inclusion criteria**

- Patients who have undergone total thyroidectomy
- Patients above the age of 18 years

**Exclusion criteria**

- Patients with chronic renal failure were excluded from the study
- Known cases of hypoparathyroidism were excluded from the study
- Patients with hypocalcemia due to any cause were excluded from the study
- Patients who were planned for modified radical neck dissection along with total thyroidectomy were excluded from the study

**Outcome measures**

*Pre-operative:* Serum calcium, serum albumin and parathyroid hormone level

*Post-operative:* Parathyroid hormone levels was assessed 1hour after total thyroidectomy. Serum calcium was assessed on post-operative day 1, 2, 3 and 4.

A serum calcium value of 8.9 to 10.6mg/dl was considered normal. Any patient with even a single postoperative calcium level of less than 8.9mg/dl was considered biochemically hypocalcaemic. Patients were evaluated for symptoms of hypocalcaemia (paraesthesia, numbness, muscle cramps and perioral numbness) and these patients were considered clinically hypocalcaemic.

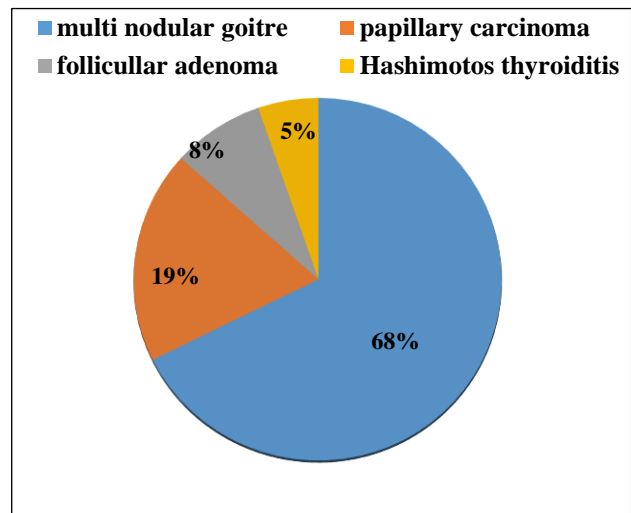
**Statistical methods**

IBM SPSS 20.0 software was used for statistical analysis. ROC curve was used to determine the cut-off value with highest sensitivity and specificity in predicting post-operative hypocalcaemia. Simple linear regression

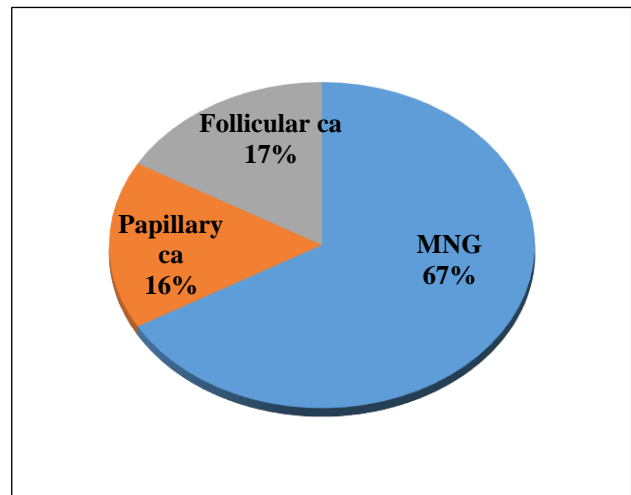
analysis was used to assess the ability of parathyroid hormone levels in predicting post op hypocalcaemia.

**RESULTS**

Out of 48 patients who underwent total thyroidectomy, 5 patients had preoperative hypocalcemia and were excluded from the study. For 43 patients who were considered, preoperative serum calcium, albumin and parathyroid hormone levels were done, and post-operative parathyroid hormone assay was performed 1 hour after total thyroidectomy and serum calcium levels calculated on post-operative day 1,2,3 and 4.



**Figure 1: Depicting disease distribution in females.**



**Figure 2: Depicting disease distribution in males.**

**Age and sex distribution**

Among 43 patients, 7 patients (16%) were between age group of 21-30 years;15 patients (35%) were between 31-40 years; 10 patients (24%) were between 41-50 years; 8 patients (18%) were between 51-60 years and 3 patients (7%) were between age group of 61-70 years.

Of 37 patients 25 were diagnosed with multinodular goiter (68%), 3 with Hashimoto's thyroiditis (8%), 7 with papillary carcinoma (19%) and 2 with follicular adenoma (5%) (Figure 1).

Of 6 male patients 4 (67%) patients had multinodular goiter (mng), 1 patient papillary carcinoma of thyroid and 1 patient had invasive follicular carcinoma (Figure 2). Of 43 patients, 37 (86%) patients were females.

**Proportion of patients developing hypocalcemia**

Normal range of parathyroid hormone (PTH) is 15-65pg/ml. Of the 43 patients, 35 developed hypocalcemia. Among 35 patients, 20 patients had symptomatic hypocalcemia. Fifteen patients had biochemical hypocalcemia. Among the 20 patients who developed symptomatic hypocalcemia, 19 patients had post-operative parathyroid hormone level (1 hour after total thyroidectomy) less than 15pg/ml. One patient had symptomatic hypocalcemia with post-operative parathyroid hormone level (1 hour after total thyroidectomy) more than 15pg/ml. Two patients were normocalcaemic in patients who had post-operative parathyroid hormone level (1 hour after total thyroidectomy) less than 15pg/ml. Fourteen patients were normocalcaemic in patients who had post-operative parathyroid hormone level (1 hour after total thyroidectomy) more than 15pg/ml.

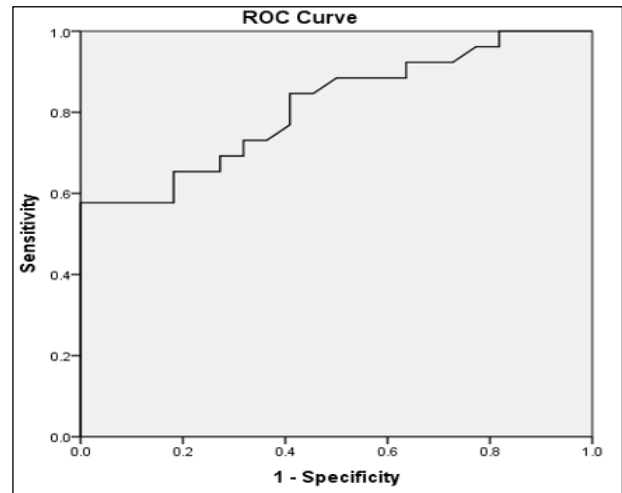
Among the patients who had symptomatic hypocalcemia (20), 19 patients had more than 75% drop in post-operative parathyroid hormone (1 hour after total thyroidectomy). Therefore, sensitivity of parathyroid hormone drops by 75% in predicting hypocalcemia is 95%. Fifty percentage drops in parathyroid hormone levels is a sensitive predictor of hypocalcemia. The selection of 15.1pg/ml as PTH level cutoff level irrespective of symptoms with 93.7% sensitivity and 91.6% specificity (Table 1).

**Table 1: Sensitivity and specificity of PTH levels in symptomatic hypocalcemia patients.**

Parathyroid hormone level (pg/ml)	Sensitivity	Specificity
19.45	73%	64%
18.15	73%	69%
17.95	69%	69%
16.65	69%	73%
14.95	65%	82%
11.05	57%	100%

Area under the curve is in a receiver operating characteristic (ROC) curve is 81.4% giving a positive predictive value of 56.99% to 83.31% and a negative predictive value of 49.63% to 78.11% (Figure 3). Hospital stay of the post total thyroidectomy who were

normocalcaemic was 4-5 days whereas those who were hypocalcaemic was 8-10 days.



**Figure 3: Receiver operation characteristic curve with area under the curve 81.4%.**

**DISCUSSION**

Hypocalcaemia is one of the most common complication following total thyroidectomy. Early identification of patients at risk of hypocalcaemia would allow for prophylactic treatment, thus avoiding the development of symptomatic hypocalcaemia and need for prolonged hospital stay. Conversely, patients who are not at risk can be spared repeated blood tests and can safely be discharged without fear of returning with hypocalcaemia.<sup>1</sup>

In this study, parathyroid hormone assay done in 43 patients 1 hour after total thyroidectomy had sensitivity of 93.7% sensitivity and 91.6% specificity of predicting biochemical hypocalcaemia at level of 15.1pg/ml. At 12pg/ml sensitivity of parathyroid hormone in predicting symptomatic hypocalcaemia was 61% and specificity was 92%. It was found that patients who had PTH at 1 hour <9pg/ml had symptomatic hypocalcaemia and can be started on prophylactic calcium supplementation.

Studies conducted have shown that PTH at 1hour is the best predictor for predicting hypocalcaemia since hypocalcaemia may develop 48hours after surgery. Parathyroid hormone (PTH) is secreted by the parathyroid glands in response to serum ionized calcium levels. The half-life of intact PTH is measured in 1-4 minutes and can be reliably assayed.<sup>2</sup>

In a study conducted by Awad and Roger in November 2011 in McGill University which stated PTH levels at 1-hour post-surgery (PTH-1) was accurate predictor of 24-hour biochemical hypocalcaemia. They measured serum calcium and serum PTH at 1,6,24 hrs. respectively. Out of 149 patients were studied of which 38 developed biochemical hypocalcaemia. In 34 of 38 patients had

serum PTH-1 levels less than 15 (Normal 15-65pg/ml). The study concluded serum PTH-1 better predictor than serum calcium.<sup>3</sup>

Trun LE in 2014 conducted study at university of Manitoba Canada, on 125 post thyroidectomy patients and measured serum PTH at 1hr post-surgery. In 31 patients had serum PTH <12pg/ml at 1hour and were considered high risk and supplemented with calcium but 5 developed hypocalcaemia. In 94 patients had serum PTH >12pg/ml at 1hour and were considered low risk but 2 developed hypocalcaemia. Study emphasized the need for considering other factors like hypomagnesemia. Study concluded serum PTH-1 useful for stratifying into low and high risk.<sup>4</sup>

Pattou et al found that a postoperative PTH level of 12pg/ml or less was a good predictor of hypocalcaemia, but they did not state how long after surgery PTH values were obtained.<sup>5</sup> Lombardi and colleagues found greater precision with measurements taken at 4 and 6 hours, with an overall accuracy of 98%.<sup>6</sup> Lam and Kerr et al reported that all patients with a PTH level less than 8pg/ml measured 1 hour after the surgery became symptomatic hypocalcaemic.<sup>7</sup>

Higgins and colleagues demonstrated that 64% of those patients who subsequently required calcium supplementation had a decrease in PTH levels greater than 75% from baseline 20 minutes after surgery. Seventy-four percentage of those who did not need calcium supplementation demonstrated a decrease of less than 75% from baseline.<sup>8</sup> The wide variability of the predictors for the development of hypocalcaemia across centers suggests that the measurement of PTH at any time in the postoperative period may be a reliable predictor of hypocalcaemia.<sup>9</sup>

## CONCLUSION

From the present study it can be concluded that a single 1-hour post-thyroidectomy parathyroid hormone level (<15pg/ml) is a valuable tool for stratifying patients as to their level of risk for developing hypocalcaemia. Patient with post-operative parathyroid hormone level <9pg/ml or with 75% drop in parathyroid hormone level can be supplemented with prophylactic calcium.

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