

# Pre and Postoperative Serum Parathyroid Hormone, Calcium and Magnesium Levels in Thyroidectomy Patients in Tertiary Care Hospital of Southern India: A Prospective Observational Study

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## ABSTRACT

**Introduction:** Thyroidectomy has been established as the preferred operation for various thyroid disorders in various forms, ranging from hemithyroidectomy, subtotal to total thyroidectomy. Postoperative hypocalcaemia is one of the most common complications that is observed in patients who undergo total thyroidectomy. To minimise the postoperative complications and to minimise hospital stay and early discharge, it is important to predict patients at risk of developing hypocalcaemia. Measurements of Parathyroid Hormone (PTH) in the immediate postoperative period along with serum calcium are useful and reliable methods.

**Aim:** To determine the risk of post total thyroidectomy by measuring PTH level after total thyroidectomy and compare serum calcium and magnesium levels pre and two hours post total thyroidectomy.

**Materials and Methods:** A prospective observational study was conducted on 34 patients, who underwent total thyroidectomy, from October 2018- May 2020. Preoperative calcium, magnesium and PTH were compared with postoperative calcium, magnesium

and PTH. All data were analysed using Statistical Package for the Social Sciences (SPSS) for Windows, Version 22.0. Paired t-test was used to compare and correlation was found.

**Results:** Present study included 6 males (17.6%) and 28 females (82.4%), there was statistically significant difference between postoperative calcium levels in total thyroidectomy without central neck dissection (mean of 8.36 mg/dL) and postoperative calcium levels in total thyroidectomy with neck dissection (mean of 7.67 mg/dL). There was a significant statistical association between postoperative calcium and postoperative PTH levels ( $p < 0.001$ ). Present study observed significant positive correlation coefficient ( $r = 0.698$ ) and a high level of significance ( $p < 0.001$ ) for postoperative calcium and postoperative PTH. Present study showed no definitive correlation between postoperative serum magnesium and calcium levels.

**Conclusion:** For predicting the risk of hypocalcaemia after thyroidectomy, it is more reliable to measure the serum PTH level before and after operation and compare the reduction level of percentage of PTH drop for predicting the risk of hypocalcaemia.

**Keywords:** Hypocalcaemia, Hypomagnesaemia, Hypoparathyroidism

## INTRODUCTION

Thyroidectomy in the form of hemi-thyroidectomy, subtotal to total thyroidectomy has been commonly performed for various thyroid diseases. Complications of total thyroidectomy include haemorrhage, injury to recurrent laryngeal nerve and hypocalcaemia. Postoperative hypocalcaemia is one of the most common complications that causes severe symptoms and increases hospital stay [1]. Incidence rates of postoperative hypocalcaemia vary from 1.6-50% according to some studies [1-3]. Serum calcium level monitoring is one of main reasons that prolongs hospital stay once the risk of other complications of surgery like haematoma and airway obstruction have been ruled out [2]. To minimise the postoperative complications and to minimise hospital stay and early discharge, it is important to predict patients at risk of developing hypocalcaemia. Measurements of PTH in the immediate postoperative period along with serum calcium is a reliable method.

Hypomagnesaemia has been associated with hypocalcaemia. Magnesium also plays an important role in calcium homeostasis via stimulation of PTH secretion, modulation of PTH receptor sensitivity and modulates renal calcium excretion. However, there is little data available regarding impact of postoperative magnesium levels on serum calcium after thyroidectomy [3].

Even though many current studies suggest the use of PTH as early predictor of hypocalcaemia and hypomagnesaemia due to variation in test standards and difference in the duration postoperatively when to measure the PTH [2,3]. It has not been followed universally.

Present study aims to determine whether measurement of PTH level in preoperative and immediate postoperative period (within two hours) in patients undergoing total thyroidectomy, could predict hypocalcaemia and hypomagnesaemia, and to standardise the test to predict the hypocalcaemia and hypomagnesaemia postoperatively.

## MATERIALS AND METHODS

A prospective observational study was conducted in tertiary care hospital of Southern India from October 2018 to May 2020. After obtaining approval from the Institutional Ethical Committee (IEC) (YEC2/2018/96) study was conducted. Verbal and written informed consent was obtained for all participants at the time of enrollment.

**Inclusion criteria:** Patients more than 18 years of age, admitted and diagnosed with thyroid disorder and requiring total thyroidectomy.

**Exclusion criteria:** Patients who did not give consent for the study, patients who had undergone thyroid surgery or neck irradiation in the past, patients who had renal dysfunction, patients who had

concomitant parathyroid disease, patients who were already on calcium supplementation.

### Study Procedure

Each patient underwent preoperative evaluation of serum calcium, magnesium and PTH. Open total thyroidectomy was done in all 34 patients. Total thyroidectomy with central lymph node dissection was performed in six patients. In each procedure, the operating surgeon attempted to identify all parathyroid glands and assess their individual viability. Postoperative serum calcium, magnesium and PTH were checked two hours after surgery. Hypocalcaemia is defined as serum calcium of <8.4 mg/dL [4]. Patients with symptomatic hypocalcaemia were those with complaints of paraesthesia, perioral numbness, and muscle cramps. All patients were checked for signs and symptoms of hypocalcaemia. All patients with signs or symptoms of hypocalcaemia, as well as those patients with serum calcium <8.4 mg/dL, were treated with oral and/or intravenous calcium. Patients were started on thrice daily with oral calcium citrate 500 mg on postoperative day 1 and continued on this supplementation at discharge.

### STATISTICAL ANALYSIS

Statistical analysis of continuous data was performed using paired t-tests. Categorical data were analysed using either Fisher's-exact tests or Chi-square tests as appropriate. The p-values <0.05 were considered statistically significant. Descriptive statistics of the explanatory and outcome variables were calculated by mean, Standard Deviation (SD) for quantitative variables, frequency and proportions for qualitative variables. Analysis of Variance (ANOVA) test was applied to test the statistical significance for more than two groups for quantitative data. Pearson's correlation was done to calculate the correlation between postoperative calcium, magnesium and PTH levels.

### RESULTS

In present study, majority of patients were in the age group of 51-60 years (32.4%) [Table/Fig-1]. Among the 34 patients, 6 were males (17.6%) and 28 were females (82.4%), proving the prevalence of thyroid disease being more in females than males [Table/Fig-2].

Age group (years)	Frequency (N)	Percentage (%)
≤30	5	14.7
31-40	8	23.5
41-50	8	23.5
51-60	11	32.4
>60	2	5.9
Total	34	100.0

[Table/Fig-1]: Distribution of the study subjects according to age group.

Parameters	Frequency (N)	Percentage (%)
<b>Sex</b>		
Male	6	17.6
Female	28	82.4
Total	34	100
<b>Postoperative diagnosis</b>		
Benign follicular nodule	2	5.88
Hashimoto thyroiditis	3	8.83
Multinodular goiter	11	32.35
Follicular carcinoma of thyroid	1	2.94
Medullary carcinoma of thyroid	1	2.94
Papillary carcinoma of thyroid	16	47.06
<b>Procedure</b>		
Total thyroidectomy	28	82.4
Total thyroidectomy with neck dissection	6	17.6

[Table/Fig-2]: Patient characteristics (N=34).

According to the postoperative diagnosis, 16 (47.06%) patients were diagnosed with papillary carcinoma of thyroid [Table/Fig-2]. Using the Pearson's correlation between postoperative calcium, magnesium and PTH levels, a significant positive correlation coefficient, r=0.698 and a high level of significance, p<0.001 for postoperative calcium and postoperative PTH was observed [Table/Fig-3].

Pearson's correlation		Post calcium (mg/dL)	Post magnesium (mg/dL)	Post PTH
Post calcium	r-value	1	0.255	<b>0.698</b>
	p-value		0.146	<b>&lt;0.001</b>
	N	34	34	34
Post magnesium	r-value	0.255	1	0.249
	p-value	0.146		0.156
	N	34	34	34
Post PTH	r-value	0.698	0.249	1
	p-value	<0.001	0.156	
	N	34	34	34

[Table/Fig-3]: Pearson's correlation between postoperative calcium, magnesium and PTH levels.

A p-value <0.05 is statistically significant

Analysis of the postoperative calcium, postoperative magnesium and postoperative PTH with the final diagnosis was done [Table/Fig-4], there was no statistically significance difference found between the postoperative calcium, postoperative magnesium and postoperative PTH levels with the diagnosis.

Parameters	Diagnosis	N	Mean	Std. Dev	F value	p-value*
Post calcium (mg/dL)	Benign follicular nodule	2	7.50	0.707	0.612	0.691
	Follicular carcinoma of thyroid	1	8.00			
	Hashimoto's thyroiditis	3	8.33	0.577		
	Medullary carcinoma of thyroid	1	8.00			
	Multinodular goitre	11	8.45	0.688		
	Papillary carcinoma of thyroid	16	8.19	0.834		
	Total	34	8.24	0.741		
Post magnesium (mg/dL)	Benign follicular nodule	2	1.50	0.707	1.520	0.216
	Follicular carcinoma of thyroid	1	1.00			
	Hashimoto's thyroiditis	3	2.00	0.000		
	Medullary carcinoma of thyroid	1	2.00			
	Multinodular goitre	11	1.82	0.405		
	Papillary carcinoma of thyroid	16	1.88	0.342		
	Total	34	1.82	0.387		
Post PTH (pg/mL)	Benign follicular nodule	2	8.50	6.364	2.408	0.062
	Follicular carcinoma of thyroid	1	14.00			
	Hashimoto's thyroiditis	3	15.33	5.132		
	Medullary carcinoma of thyroid	1	31.00			
	Multinodular goitre	11	28.18	9.611		
	Papillary carcinoma of thyroid	16	21.63	9.811		
	Total	34	22.47	10.326		

[Table/Fig-4]: Postoperative calcium, magnesium and PTH according to diagnosis.

\*ANOVA

A statistically significant difference between postoperative calcium levels in total thyroidectomy and postoperative calcium levels in total thyroidectomy with central neck dissection was found [Table/Fig-5], proving there is higher risk of postoperative hypocalcaemia

following total thyroidectomy with central neck lymph node dissection. No similar statistically significant difference was found between postoperative magnesium or postoperative PTH levels in total thyroidectomy without central neck dissection and in patients with total thyroidectomy with central neck dissection [Table/Fig-5].

Parameters	Diagnosis	N	Mean	Std. Dev	Mean difference	p-value*
Post calcium (mg/dL)	Total thyroidectomy	28	8.36	0.678	0.690	0.036
	Thyroidectomy with neck dissection	6	7.67	0.816		
Post magnesium	Total thyroidectomy	28	1.82	0.390	-0.012	0.967
	Thyroidectomy with neck dissection	6	1.83	0.408		
Post PTH	Total thyroidectomy	28	23.43	10.528	5.429	0.249
	Thyroidectomy with neck dissection	6	18.00	8.718		

**[Table/Fig-5]:** Comparison of mean postoperative PTH, calcium, magnesium levels with procedure.

\*Unpaired t-test; A p-value <0.05 is statistically significant

Postoperatively, 15 patients (44.1%) patients developed hypocalcaemia, of which 11 patients were symptomatic and required medical management, 13 patients (38.2%) developed hypomagnesaemia of which 12 had low PTH values.

On comparing the postoperative PTH values with postoperative calcium values, it was seen that 11 (73.33%) patients out of the 15 patients, who developed hypocalcaemia also had low PTH levels. Using Yate's Chi-square test, the p-value was <0.001 which showed a significant statistical association between postoperative calcium and postoperative PTH levels.

We compared the postoperative PTH values with postoperative magnesium values. It was seen that 7 (53.85%) patients out of the 13 patients, who developed hypomagnesaemia also had low PTH levels and 6 (46.15%) patients out of 13 patients developed hypomagnesaemia had a normal PTH level. Using Yate's Chi-square test the p-value was 0.158 which shows no statistically significant association between postoperative magnesium and postoperative PTH levels.

## DISCUSSION

In present study, out of 34 patients, 6 were males (17.6%) and 28 were females (82.4%), proving the prevalence of thyroid disease being more in females than males. Similar to other studies by Lombardi CP et al., Garrahy A et al., and Lo CY et al., who had higher prevalence of thyroid diseases in females [1,3,5]. In Lombardi CP et al., out of 53 patients 48 (90.5%) were females and 5 (9.5%) were males; Garrahy A et al., had 168 (83.5%) female and 33 (16.5%) male patients out of 201 individuals included in the study; Lo CY et al., included 13 (65%) females and 7 (35%) males in the control group (n=20) and had 78 (78%) females and 22 (22%) males in the study group (n=100) [1,3,5].

Present study shows a significant statistical association between postoperative calcium and postoperative PTH levels (p<0.001). This was in line with other studies like Lombardi CP et al., [1]. They concluded that a single intraoperative measurement of PTH can predict which patients are prone to postoperative hypocalcaemia and necessitate calcium supplementation and this can also predict which patients would be eligible for early discharge [1]. Payne RJ et al., also concluded that evaluation of PTH and corrected calcium levels six hours post-thyroidectomy can accurately predict the trend of serum calcium and can enable same day discharges for most patients [2].

In present study, higher risk of postoperative hypocalcaemia following total thyroidectomy with lymph node dissection of the neck was observed which was in line with the study done by Wilson RB et al., which showed that parathyroid resection and neck dissection were risk factors for developing hypocalcaemia

[6]. Nair CG et al., also demonstrated similar findings with higher incidence of hypocalcaemia associated with total thyroidectomy with central compartment dissection [7]. This shows that better surgical techniques and skills are required when performing total thyroidectomy with neck lymph node dissection to prevent injury to parathyroid glands. Further studies regarding surgeon's expertise, experience, skill and newer techniques to identify and preserve parathyroid might be required for total thyroidectomy with neck lymph node dissection.

Out of 34 patients, 15 (44.1%) patients developed hypocalcaemia in present study, out of which 11 patients were symptomatic and required medical line of management. Thirteen patients developed hypomagnesaemia and 12 patients developed hypoparathyroidism. However, none developed permanent hypocalcaemia. Similar results were seen in study conducted by Wilson RB et al., were 18 (36%) patients out of 50 individuals developed symptomatic temporary hypocalcaemia, requiring oral and intravenous calcium supplementation [6]. Cherian AJ et al., had 25 (50%) patients had clinical features of hypocalcaemia postoperatively. A 21/25 patients (84%) had either symptoms or signs present. Among these patients, hypomagnesaemia was present in 19/21 (90.5%), whereas hypocalcaemia was present in 11/21 (52.4%) patients. A 4/25 (16%) patients had both signs and symptoms of hypocalcaemia and had both hypocalcaemia and hypomagnesaemia [8].

Present study also showed there was no definitive correlation between serum magnesium and serum calcium post total thyroidectomy. This was in line with studies by Wang X et al., mentioning that postoperative hypomagnesaemia was not an independent predictor of hypocalcaemia after total thyroidectomy and it seems to be pointless to regularly screen the magnesium levels before and after thyroid surgery [9]. Study conducted by Sousa AD et al., had similar results [10]. However, retrospective study conducted by Mahmoud RR et al., showed that hypomagnesaemia was associated with hypocalcaemia and found similarities between the curves of calcium and magnesium in Group 1 (patients with normal calcium) and Group 2 (patients with hypocalcaemia) [11]; but PTH level fall was noted in both the groups and thus could not explain correlation of PTH to magnesium or calcium. In present study, there was no definitive correlation between serum PTH and serum magnesium. Further studies might be required to prove or disprove these correlations.

## Limitation(s)

Sample size of the study was small. Larger study with more number of individuals may be required. Present study was based on single value of PTH and magnesium levels done two hours postoperatively. Serial values of PTH and magnesium would (have increased the cost but) have provided a better correlation and better timing of performing the blood values.

## CONCLUSION(S)

To conclude, there is a definitive relation to the levels of serum PTH (two hours) post total thyroidectomy with the level of serum calcium. There was no significant correlation between postoperative magnesium levels with calcium or PTH levels. Postoperative normal PTH values may facilitate early discharge in patients undergoing total thyroidectomy without having any other complications.

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