

The Incidence of Hypocalcemia following Total Thyroidectomy: A Retrospective Study**Ramakrishna Bezawada^{a*}, Narendra M C^a, Mutheeswaraiyah Y^a, Rukmangadha N^b**^aDepartment of General Surgery, Sri Venkateswara Institute of Medical Sciences, Sri Padmavathi Medical College for Women, Tirupati, India.^bDepartment of Pathology, Sri Venkateswara Institute of Medical Sciences, Sri Padmavathi Medical College for Women, Tirupati, India.**Abstract**

Background: Hypocalcemia is one of the major complications following total thyroidectomy that can range in severity from asymptomatic to an acute life-threatening condition. Post-operative hypocalcemia is one of the causes of increased hospital stays and expenses for treatment.

Objectives: To evaluate the hypocalcaemia in total thyroidectomy patients concerning the age and gender of patients, and also to evaluate the association between various histological types of thyroid diseases and hypocalcemia.

Patients and methods: A retrospective study was conducted to estimate hypocalcaemia in 81 patients who underwent total thyroidectomy at a tertiary care medical institute in Southern India, from January 2016 to December 2016. Clinical, laboratory, radiological, and histopathology data were collected and assessed from the medical records department of the hospital.

Results: In this study, all the hypocalcemic patients were females with a mean age of 40.36 Years. 43.2% developed temporary and 3.7% permanent hypocalcemia. Temporary hypocalcemia was more common in adenomatous goiter and permanent hypocalcemia in malignant thyroid diseases.

Conclusion: We didn't find any association between hypocalcemia and advancing age. Similarly, we didn't find any association between temporary hypocalcemia to histopathological diagnosis but all the patients with permanent hypocalcemia had malignant disease.

Keywords: Total thyroidectomy; Hypocalcemia; Corrected calcium; Serum calcium.

DOI: 10.21608/svuijm.2022.165850.1425

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Received: 3 October, 2022.

Revised: 4 December, 2022.

Accepted: 7 December, 2022.

Cite this article as: Ramakrishna Bezawada, Narendra M C, Mutheeswaraiyah Y, Rukmangadha N. (2023). The Incidence of Hypocalcemia following Total Thyroidectomy: A Retrospective Study. *SVU-International Journal of Medical Sciences*. Vol.6, Issue 1, pp: 457- 464 .

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Introduction

Hypocalcemia is one of the major complications following total thyroidectomy that can range in severity from asymptomatic to presenting as an acute life-threatening condition (**Fong and Khan, 2012**). Post-operative hypocalcemia is one of the causes of increased hospital stays and the cost of treatment (**Bhattacharyya and Fried, 2002**). The major cause of hypocalcemia following surgery is secondary hypoparathyroidism which usually follows injury and/or devascularization of the parathyroid glands, accidental parathyroidectomy, and failure to do auto-transplantation (**Abboud et al., 2002**). The clinical symptoms of hypocalcemia are normally seen 24 to 48 hours after the total thyroidectomy procedure (**Sperlongano et al., 2014**).

Post-operative hypocalcemia persisting for 6 months is considered temporary hypocalcemia and if it is lasting for more than six months is considered permanent hypocalcemia (**Abboud et al., 2010**). The frequency of transient hypocalcemia following total thyroidectomy is between 19 to 38%, whereas permanent hypocalcemia varies between 0 to 3% (**Edafe et al., 2014**).

Ionized calcium is an important portion of serum total calcium (**Payne et al., 1979**). Measuring ionized calcium is expensive, so ionized calcium concentration is calculated by the concentrations of calcium, protein, or albumin (**Gouri and Dekaken, 2012**), as Corrected Calcium (mg/dl) = Total Calcium (mg/dl) + 0.8 x [4 – Serum Albumin (g/dl)] (**Siyama and Klachko, 2013**).

Adjusted calcium is also used for calcium correction in hypocalcemia using this formula i.e.

Adjusted Calcium = Calcium (mg/100 ml) - Albumin (g/100 ml) + 4 (**Payne et al., 1973**).

Symptomatic hypocalcaemia is a medical emergency that should be treated with

intravenous administration of 10 ml of 10% calcium gluconate in 100 ml 5% dextrose over 5-10 minutes and this should be repeated until the resolution of symptoms. It should be followed by oral calcium and Calcitriol supplementation until the serum calcium level returns to normal.

This study aims to evaluate post-operative hypocalcemia following total thyroidectomy concerning age, gender, and histopathological diagnosis. The current study aimed to evaluate hypocalcaemia following total thyroidectomy concerning age and gender. Additionally, to evaluate the association between various histological types of thyroid diseases and hypocalcemia.

Patients and methods

A retrospective study was conducted to evaluate hypocalcaemia in the patients who underwent total thyroidectomy in the department of General surgery at Sri Venkateswara Institute of Medical Sciences, Sri Padmavathi Medical College for Women, Tirupathi, India, from January 2016 to December 2016.

Inclusion criteria

1. All the patients who underwent total thyroidectomy from January 2016 to December 2016.
2. Age more than 18 years.

Exclusion criteria

1. Patients who underwent hemithyroidectomy, subtotal, and near-total thyroidectomy.
2. Patients with pre-existed parathyroid pathologies and symptoms of hypocalcemia or on calcium supplementation.

Methodology

In this retrospective study, the following details of data were collected from the medical records department of the hospital, including details of history, clinical examination, clinical diagnosis, thyroid function test, fine needle aspiration cytology (FNAC), neck ultrasonography,

intraoperative findings of total thyroidectomy, post-operative diagnosis, post-operative serum calcium, serum phosphorus, serum albumin, corrected serum calcium, clinical signs of hypocalcemia, treatment details of hypocalcemia, biopsy reports and 6 months follow up of hypocalcemia patients and their treatment details. Positive Trousseau sign and corrected serum calcium value less than 8.5 mg/dL are used to diagnose clinical and biochemical hypocalcemia respectively. Post-operative hypocalcemia persisting for 6 months is considered temporary hypocalcemia and lasting for more than six months is considered permanent hypocalcemia.

Ethical issues: Ethical clearance for the retrospective study was taken from the institutional ethics committee of Sri Venkateswara Institute of Medical Sciences, Sri Padmavathi Medical College for Women, Tirupathi, India.

Statistical analysis

Data from 81 patients were collected and entered into the MS Excel sheet and analyzed using IBM-SPSS software version 21. The following descriptive statistics like frequencies and percentages, means, standard deviations, and ranges were

calculated. The Chi-square test and student's t-test are used to analyze the significance of discrete and continuous data. A p-value of equal to or less than 0.05 is taken as the significance level.

Results

In this study, 81 patients underwent total thyroidectomy, 85% of our patients were females. The mean age was 40.36 ± 10.67 years. Most of the patients were between 41 to 50 years of age (38.27%) followed by 31 to 40 years of age (33.33%). The majority of patients were ≤ 50 years of age (87.65%). Multinodular goiter was the most common pre-operative indication for total thyroidectomy followed by carcinoma thyroid and thyrotoxicosis. The majority belongs to the non-toxic goiter group compared to the toxic goiter. Among the postoperative histopathological diagnoses most were adenomatous goiter followed by a follicular variant of papillary carcinoma, 48 (59.25%) patients had benign and 33 (40.74%) had a malignant disease. The mean post-operative serum corrected calcium was 8.64 ± 0.56 mg/dl. 38 patients developed hypocalcemia, among them 35 (43.21%) had temporary and 3 (3.7%) had permanent hypocalcemia, (Table. 1).

Table 1. Patient demographic and other characteristics

	Number of patients (N=81)
Gender	
• Women	69(85%)
• Men	12 (15%)
Age group	
• 18 -30 years	13(16.04%)
• 31-40 years	27(33.33%)
• 41-50years	31(38.27%)
• 51-60years	7(8.64%)
• 61-70years	3 (3.7%)
• ≤ 50 years	71(87.65%)
• >50 years	10(12.34%)
Mean age \pmSD	40.36 \pm 10.67 years
Preoperative diagnosis	

• Multinodular goiter	56(69.13%)
• Thyrotoxicosis	7(8.64%)
• carcinoma thyroid	18(22.22%)
Histopathology	
Adenomatous goiter	37(45.67%)
Graves' disease	6(7.4%)
Follicular adenoma	2(2.46%)
Hashimoto's thyroiditis	3(3.7%)
Follicular variant of papillary carcinoma	18(22.22%)
Papillary carcinoma	12(14.81%)
Medullary carcinoma	2(2.46%)
Follicular carcinoma	1(1.23%)
Benign	48 (59.25%)
Malignant	33(40.74%)
Toxic goiter	6(7.41%)
Non-toxic goiter	75(92.59%)
With hypocalcemia	38(46.91%)
Without hypocalcemia	43(53.09%)
Temporary hypocalcemia	35(43.21%)
Permanent hypocalcemia	3(3.7%)
Mean corrected calcium±SD	8.64±0.56

In this study, all the hypocalcemic patients were females, with a mean age of 38.74±9.50 years. The majority of hypocalcemic patients were distributed between the 31 to 50 years age group (78.95%). Only 2 (2.47%) patients older than 50 years had hypocalcemia whereas 36(44.44%) patients of ≤ 50 years had

hypocalcemia (p = 0.068). 20 (24.69%) patients with benign thyroid and 18 (22.22%) patients with malignant thyroid diseases had hypocalcemia (p = 0.253). 2 (2.47%) patients of toxic and 36 (44.44%) non-toxic goiter patients had hypocalcemia (p=0.48), (**Table. 2**).

Table 2. Patient characteristics concerning serum calcium levels

	Patients with Hypocalcemia N(%)	Patients without hypocalcemia (%)	P-value
Gender			
• Women	38(46.91%)	31(38.27%)	Not applicable
• Men	0(0%)	12(14.81%)	
Mean age ±SD	38.74±9.50	41.79±11.52	0.741 (Chi-square 26.49)
Age group			
• 18 -30 years	6(7.4%)	7(8.64%)	0.350 (Chi-square 4.436)
• 31-40 years	15(18.51%)	12(14.81%)	
• 41-50years	15(18.51%)	16(19.75%)	
• 51-60years	2(2.46%)	5(6.17%)	
• 61-70years	0(0%)	3(3.70%)	
• ≤ 50 years	36 (44.44%)	35(43.21%)	0.068 (Chi-square 3.31)

• >50 years	2 (2.47%)	8(9.88%)	
Histopathology			
• Benign	20(24.69%)	28(34.57%)	0.253 (Chi-square 1.30)
• Malignant	18(22.22%)	15((18.52%)	
• Toxic Goitre	2(2.47%)	4(4.94%)	0.49 (Chi-square 0.48)
• Non-toxic goiter	36(44.44%)	39(48.14%)	

Among the 81 patients, 3 had permanent hypocalcemia and all of them were malignant, whereas temporary

hypocalcemia was observed more in benign diseases like adenomatous goiter, (Table.3).

Table 3 Histopathological diagnosis concerning calcium level

Histopathology	Patients with Temporary Hypocalcemia N (%)	Patients with Permanent hypocalcemia N(%)	Patients without Hypocalcemia N(%)	P-value
Adenomatous goiter	16 (19.75%)	0	21(25.93%)	0.209 (Chi-square 17.94)
Graves' disease	2 (2.46%)	0	4(4.94%)	
Follicular adenoma	1(1.23%)	0	1(1.23%)	
Hashimoto's thyroiditis	1 (1.23%)	0	2(2.47%)	
Follicular variant of papillary carcinoma	10(12.35%)	1(1.23%)	7(8.64%)	
Papillary carcinoma	5 (6.17%)	1(1.23%)	6(7.41%)	
Medullary carcinoma	0	1(1.23%)	1(1.23%)	
Follicular carcinoma	0	0	1(1.23%)	

Discussion

Hypocalcemia is one of the major postoperative complications of total thyroidectomy which can affect the quality of life significantly according to Kolly et al. (2017). In this study, the distribution of hypocalcemia following total thyroidectomy was 46.9% and permanent hypocalcemia was 3.7 %. Edafe et al. (2014) reported that temporary hypocalcemia following total thyroidectomy was 27(19-28)% and permanent hypocalcemia was 1(0-3)%. Eismontas et al. (2018) showed hypocalcemia following total thyroidectomy was 64.2% Arumugam et al. (2017) got the incidence of postoperative hypocalcemia was approximately 35%. Asari et al. (2008) documented an incidence of temporary and permanent hypocalcemia at 24% and 1%

respectively. Karamanakos et al. (2010) reported an incidence of hypocalcemia of 40.4%. Fahmy et al. (2004) documented the incidence of transient hypocalcemia was 66.66 %, while permanent hypocalcemia was 22.22 %.

In this study, 78.94 % of patients were between 31 to 50 years of age and there was no association between advancing age (>50 years) with hypocalcemia (P= 0.068). Pradeep et al. (2013) and Eismontas et al. (2018) also had shown that there is no association between age and hypocalcemia. Arumugam et al. (2017) reported that post-thyroidectomy hypocalcemia incidence was more common in the advancing age group, i.e., more than 50 years. Erbil et al. (2009) also documented that advancing age was associated with hypocalcemia.

In this study interestingly all the patients with hypocalcemia were women. **Thomusch et al. (2003)** and **Ozogul et al. (2014)** documented that hypocalcemia was significantly higher in women. **Yamashita et al. (2000)**; **Prim et al. (2001)** showed similar observations. But, **Lombardi et al. (2006)** concluded that there was no association between gender and postoperative hypocalcemia.

In this study incidence of hypocalcemia is more common in malignant diseases (54%) compared to benign diseases (41.6%) but there was no significant association ($p=0.253$). **Sakouti et al. (2010)**; **Sousa et al. (2012)**; **Babu et al. (2017)** documented that high incidence of hypocalcemia after total thyroidectomy for malignant diseases.

In this study, there was no increased incidence of hypocalcemia in thyrotoxicosis ($p = 0.49$). Similar results were also seen in a study conducted by **Eismontas et al. (2018)** on long-standing thyrotoxicosis. **Thomusch et al. (2003)** showed that both temporary and permanent hypocalcemia was more common following total thyroidectomy for Grave's thyroiditis. **Nair et al. (2013)** also reported a higher association between thyrotoxicosis and postoperative hypocalcemia.

Conclusion

Hypocalcemia following total thyroidectomy was more common in women between the 31 to 50 years of age group. Temporary hypocalcemia was 43.2 % and permanent hypocalcemia was 3.7%. We didn't find any association between hypocalcemia and the advancing age > 50 years. Similarly, we didn't find any association between temporary hypocalcemia and histopathological diagnosis, but all the patients with permanent hypocalcemia had malignant disease. Proper identification and meticulous dissection are required to preserve parathyroids during all total thyroidectomy

procedures, especially for malignant conditions to prevent postoperative hypocalcemia.

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