

FREQUENCY OF ASYMPTOMATIC HYPOCALCEMIA IN POST-THYROIDECTOMY PATIENTS: AN EXPERIENCE IN TERTIARY CARE HOSPITAL

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Abstract: Hypocalcemia is a frequent and clinically significant complication following total thyroidectomy. While most cases are transient and asymptomatic, persistent hypocalcemia can lead to prolonged hospital stays, increased healthcare costs, and reduced quality of life. Identifying the predictors of postoperative hypocalcemia is essential for early diagnosis, prevention, and management. **Objective:** To assess the incidence and predictors of hypocalcemia in patients undergoing total thyroidectomy. **Methods:** A prospective study was conducted in the Surgical Ward of Nishtar Hospital Multan from April 2024 to September 2024. A total of 100 patients with thyroid carcinoma, thyroid nodules, or thyroiditis undergoing total thyroidectomy were included in the study. Surgical factors, clinical effects, patient characteristics, and pathological variables were explored to determine their impact on post-operative thyroidectomy which was defined as a serum calcium level less than 2.1 mmol/L. **Results:** 65 (65%) patients developed postoperative hypocalcemia among which 75.4% had asymptomatic hypocalcemia. An occurrence of a thyroid storm less than 10 years before the study was significantly associated with the development of hypocalcemia ($p=0.049$). Ligation of the trunk of the left ($p=0.005$) and right inferior thyroid artery ($p<0.001$), number of parathyroid glands ($p<0.001$), and auto-transplanted PGs ($p=0.020$) were also significant risk factors of hypocalcemia. Lastly, PTH level on day 1 postop was also a strong predictor ($p<0.001$). Multivariate regression model showed old age ($p=0.032$) and female sex ($p=0.041$) as significant independent risk factors of hypocalcemia. **Conclusion:** There is a high incidence of postoperative asymptomatic hypocalcemia in patients undergoing total thyroidectomy. Patients' demographic factors including age, sex, and occurrence of thyrotoxicosis, and surgical factors including intraoperatively identified PGs, preoperative calcium and ionized calcium levels, PTH within first 24 hours postop, and ligation of the trunk of left and right inferior thyroid artery were significant risk factors.

Keywords: Hypocalcemia, Surgery, Thyroid, Thyroidectomy

Introduction

Thyroid surgery is one of the most commonly performed procedures globally. It is the primary management technique for malignant tumours and other diseases including benign multinodular goitre. Temporary or permanent hypocalcemia is a frequent complication of total thyroidectomy. Temporary hypocalcemia lasts for 6-12 months and occurs in 50-70% of patients while permanent hypocalcemia lasts more than a year occurring in 3% of patients. (1, 2).

Risk factors of hypocalcemia have been identified in thyroidectomy patients including surgical trauma, carcinoma, hyperthyroidism, incidental parathyroidectomy, retrosternal goiter, calcium and vitamin D supplements concomitant neck dissection, etc. (3, 4). The effect of age has been conflicted as it has been reported to have a positive impact on postoperative calcium levels in some studies but this hypothesis was rejected by others. (5). The risk of hypocalcemia presented higher in patients undergoing total thyroidectomy as compared to completion procedures (6). Laboratory analysis can also act as a predictor of hypocalcemia as i-PTH levels have been reported to predict hypocalcemia but its use is limited due to cost and availability (7).

This study was conducted to assess the incidence and predictors of hypocalcemia in patients undergoing total thyroidectomy.

Methodology

A prospective study was conducted in the Surgical Ward of Nishtar Hospital Multan from April 2024 to September 2024. A total of 100 patients with thyroid carcinoma, thyroid nodules, or thyroiditis undergoing total thyroidectomy were included in the study. Patients with a history of lobectomy, thyroid gland resection, hemithyroidectomy, and pathologic diagnosis of parathyroid glands were excluded. All patients provided their informed consent to become a part of the study. The ethical committee of the hospital approved the study. All procedures were performed by high-volume surgeons. Biochemical blood parameters were recorded before and after surgery by drawing blood from the peripheral vein. Surgical factors, clinical effects, patient characteristics, and pathological variables were explored to determine their impact on post-operative thyroidectomy which was defined as a serum calcium level less than 2.1 mmol/L. Laboratory tests were performed preoperatively to measure calcium



levels, thyroid hormones, ionized calcium, 25-hydroxy vitamin D, and parathyroid hormone.

The postoperative hospital stay was 48 hours. Calcium, ionized calcium, and PTH were measured within 24 hours post-op. Calcium and ionized calcium were also measured on day 2. Clinical manifestations and time of presentation of hypocalcemia were recorded. Surgical factors include intraoperative sightings of parathyroid glands, auto-transplanted parathyroid glands, and ligation of vessels leading to the thyroid gland. Oral calcium 1500-3000 mg was administered twice a day if the patient showed hypocalcemic symptoms or had a calcium level less than 2 mmol/L. Calcitriol 0.25 mcg was also given with oral calcium in high-risk patients such as auto-transplanted PGs, central neck dissection, recurrent neck surgery, PG injury during surgery, or low PTH and 25-hydroxy vitamin D postoperatively.

All data was analyzed by SPSS 24. Continuous data was processed by univariate descriptive analysis and categorical data was presented by percentage. A chi-square test was performed to assess the relationship between categorical parameters. Z-test was used to compare proportions between hypocalcemic and non-hypocalcemic patients. Predictors of hypocalcemia were assessed by binary logistic regression model which were processed into multivariate analysis to assess independent risk factors. Statistical significance was taken at <0.05.

Results

A total of 100 patients with a mean age of 56.1 ± 12.5 years were included in the study. 65 (65%) patients developed postoperative hypocalcemia among which 75.4% had asymptomatic hypocalcemia. 16% of patients with hypocalcemia showed clinical symptoms. 5% of patients showed Chvostek’s signs and 3% showed Trousseau’s signs. Decreased calcium and ionized calcium levels before surgery were significantly associated with postoperative hypocalcemia (p<0.001). Carcinoma, bilateral neck dissection, intraoperative bleeding, postoperative hematoma, and revision for bleeding did not alleviate the risk of hypocalcemia. Tables 1 and 2 show the preoperative and postoperative variables of study patients.

An occurrence of a thyroid storm less than 10 years before the study was significantly associated with the development of hypocalcemia (p=0.049). Ligation of the trunk of the left (p=0.005) and right inferior thyroid artery (p<0.001), number of parathyroid glands (p<0.001), and auto-transplanted PGs (p=0.020) were also significant risk factors of hypocalcemia. Lastly, PTH level on day 1 postop was also a strong predictor (p<0.001) (Table 3). Multivariate regression model showed old age (p=0.032) and female sex (p=0.041) as significant independent risk factors of hypocalcemia (Table 4).

Table 1: Demographic and preoperative factors

Variables	N (%)
Mean age	56.1 ± 12.5
Gender	
Male	12 (12%)
Female	88 (88%)
Mean weight	80.1 ± 16.3

Thyrotoxicosis before surgery	
None	70 (70%)
<10 years	25 (25%)
>10 years	5 (5%)
Diagnosis	
Graves’ disease	5 (5%)
Recurrent goiter	1 (1%)
Retrosternal goiter	2 (2%)
Adenomatous nodules	17 (17%)
Colloidal nodules	68 (68%)
Papillary carcinoma	20 (20%)
Follicular carcinoma	1 (1%)
Medullary carcinoma	1 (1%)
Autoimmune thyroiditis	10 (10%)
Preoperative laboratory parameters	
Calcium	2.41 ± 0.09
Ionized calcium	1.11 ± 0.10
PTH	56.67 ± 23.33
25-hydroxy Vit-D	46.30 ± 21.98
TSH	0.88 ± 1.17
FT3	4.92 ± 2.41
FT4	12.24 ± 2.76
Parathyroid glands	
0	1 (1%)
1	3 (3%)
2	25 (25%)
3	51 (51%)
4	20 (20%)
Auto-transplanted PGs	
0	85 (85%)
1	11 (11%)
2	3 (3%)
3	1 (1%)

Table 2: Postoperative data

Variables	N (%)
Hypocalcemia	65 (65%)
Asymptomatic hypocalcemia	49 (75.4%)
Symptomatic hypocalcemia	16 (24.6%)
Day 1 post-op	
Calcium	2.09 ± 0.15
Ionized calcium	1.0 ± 0.11
PTH	30.04 ± 20.50
Day 2 post-op	
Calcium	2.03 ± 0.22
Ionized calcium	0.99 ± 0.12
Complications	
Revision for bleeding	1 (1%)
Wound infection	-
Wound hematoma	3 (3%)
Intraoperative bleeding	1 (1%)
Hoarseness	4 (4%)
Recurrent one-sided laryngeal nerve paralysis	2 (2%)
Calcium and Vit D treatment	
None	40 (40%)
Day 1	4 (4%)
Day 2	9 (9%)
Day 3	2 (2%)

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On discharge	45 (45%)
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Table 3: Risk factors of postoperative hypocalcemia

Variables	OR (95%CI)	P- Value
Thyrotoxicosis before surgery		
<10 years	1.72 (0.99-2.68)	0.049
>10 years	1.0 (0.43-2.59)	0.977
Ligation of the trunk of the left inferior thyroid artery	2.11 (1.32-3.33)	0.005
Ligation of the trunk of the right inferior thyroid artery	2.43 (1.55-3.76)	<0.001
Preoperative calcium levels	0.02 (0.99-0.61)	<0.001
Preoperative ionized calcium levels	0.002 (0-0.015)	<0.001
Preoperative PTH levels	1.0 (0.98-1.0)	0.849
PTH day 1 post-op	0.98 (0.96-0.99)	<0.001
Preoperative 25-hydroxy vit-D levels	1.0 (1.0-1.01)	0.199
Preoperative TSH	1.18 (0.97-1.43)	0.2
Preoperative FT4	0.99 (0.88-1.08)	0.63
Preoperative FT3	1.0 (0.89-1.10)	0.86

Table 4: Multi-variate analysis

Variables	OR (95% CI)	P- Value
Age	1.08 (0.99-1.12)	0.032
Gender	6.0 (1.16-32.34)	0.041
Calcium day 2 post-op	0	<0.001

Discussion

This study was conducted to assess the incidence and risk factors of postoperative hypocalcemia in patients undergoing thyroidectomy. 65% of the patients developed hypocalcemia after surgery among which 75.4% had asymptomatic and 14.6% had symptomatic hypocalcemia. This incidence complied with previous literature reporting 50-70% frequency of hypocalcemia (8). The majority of hypocalcemia is asymptomatic in most patients and can only be treated with oral calcium and vitamin D (9). In the present study, 40% of patients did not receive any treatment and 15% received treatment for up to 3 days postop. Calcium and ionized calcium levels before surgery were significantly associated with postoperative hypocalcemia. Other studies also reported that patients with decreased calcium preoperatively were more likely to develop hypocalcemia (10). A meta-analysis involving over 2000 patients disagrees with our results and did not report any significant relationship between temporary hypocalcemia and preoperative calcium levels (11). An immediate reduction in calcium after total thyroidectomy increases the risk of hypocalcemia. A multi-hospital study conducted on 1150 patients revealed that a 2-3% reduction in calcium levels within 24 hours postoperatively is associated with a 94% risk of temporary hypocalcemia (12). Permanent hypocalcemia is associated with a postoperative calcium level of 1.8 mmol/L or less in the first 24 hours after surgery (13). A calcium level of 2 or less 7-24 days after surgery also increases the likelihood of permanent hypocalcemia. (14).

PTH level day 1 postop was significantly associated with hypocalcemia in the current study ($p < 0.001$). Previous literature supports this result and found that decreased PTH after surgery can increase the risk of temporary hypocalcemia by 70-100%. (15, 16). The number of

parathyroid glands was also a significant risk factor for hypocalcemia with an indirect association between the two. Identification of <2 PGs intraoperatively increased the chances of permanent hypocalcemia. However, several studies contrast these results and report a direct association between the number of PGs and temporary hypocalcemia (15, 17).

A direct significant association between auto-transplanted PGs and hypocalcemia was found in our study. Many studies back this result by stating that ≥ 1 auto-transplanted PGs, the greater the risk of hypocalcemia. (18, 19) Other studies reject any association between permanent hypocalcemia and auto-transplanted PGS. (20)

A thyroid storm less than 10 years before surgery was also a significant predictor ($p = 0.049$). However, no significant association was found between the occurrence of thyroid storm more than 10 years before the study and Graves' disease which may be due to a limited number of patients in these categories. However, several meta-analyses bind Graves' disease with a significant risk of temporary and permanent hypocalcemia (21). Multivariate analysis in our study showed old age and female sex as independent risk factors. Although no definite evidence is available to support this claim, the association of age has been reported by conflicting results in the literature (22, 23). A meta-analysis conducted in 3500 patients reported an association between females and temporary hypocalcemia.

Our study has some limitations. The sample size was limited due to which association between various variables could not be computed.

Conclusion

There is high incidence of postoperative asymptomatic hypocalcemia in patients undergoing total thyroidectomy. Patients' demographic factors including

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age, sex, and occurrence of thyrotoxicosis, and surgical factors including intraoperatively identified PGs, preoperative calcium and ionized calcium levels, PTH within first 24 hours postop, and ligation of trunk of left and right inferior thyroid artery were significant risk factors.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRBEC-NHM-034/23)

Consent for publication

Approved

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The authors declared absence of conflict of interest.

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Coordination of collaborative efforts.

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Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

Conception of Study, Final approval of manuscript.

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