

Original Article

Hypocalcaemia after Total Thyroidectomy

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Abstract

Objective: To determine whether postoperative hypocalcemia after total thyroidectomy is more frequent in malignant disease than benign disease.

Methods: This is a Cross sectional study. The sample size is 126. All the patients were selected according to the eligibility criteria by purposive sampling. Patients were analyzed for age, gender, thyroid pathology, preoperative serum calcium, postoperative serum calcium.

Results: Postoperative hypocalcemia was found in 37 (29.37%) patients. Most patients were female (Male: Female= 1: 4.2). Patients having low preoperative serum calcium had developed more postoperative hypocalcemia ($p < 0.03$). Postoperative hypocalcemia was associated with thyroid pathology ($p < 0.009$) and age ($p < 0.006$), not associated with sex ($p < 0.907$). In multivariate analysis very little association between malignant disease and postoperative hypocalcemia was found ($p < 0.07$).

Conclusion: The incidence of postoperative hypocalcemia following total thyroidectomy is 29.4% that is higher than the anticipated but is comparable to other published series. For total thyroidectomy surgeons should be aware of postoperative hypocalcemia but prophylactic calcium and vitamin D supplement is not mandatory in all cases.

Keywords: Total thyroidectomy, hypocalcemia, postoperative hypocalcemia.

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Introduction:

Complications of thyroid surgery can be classified into different ways like- early, intermediate and late; local and general; those specific to the operation. Early complications include haemorrhage, voice change, airway obstruction and temporary hypoparathyroidism. The intermediate ones include seroma formation, infection and temporary palsy of the recurrent laryngeal nerve and the external branch of the superior laryngeal nerve. Late complications include subclinical hypothyroidism, permanent hypoparathyroidism, permanent injury to the recurrent laryngeal nerve, the external branch of the superior laryngeal nerve, the cutaneous nerves C2 and C3 and the accessory nerve and a poor scar.¹

Hypocalcemia after thyroid surgery occurs due to hypofunction of parathyroid gland. Parathyroid gland dysfunction occurs due to

inadvertent excision of the gland or impaired vascularity of the gland.² The postoperative stress causing hemodilution and antidiuretic hormone secretion also lowers total serum calcium levels.^{3,4} Hungry bone syndrome may occasionally contribute to the immediate post-operative hypocalcemia.^{5,6} Sometimes calcitonin release is thought to be a cause of hypocalcemia.^{7,8}

Vascular impairment of parathyroid gland may occur during the dissection especially while securing upper pole vessels.⁹ Sometimes the parathyroid glands may be impossible to identify as they may lie beneath the thyroid capsule or completely within the thyroid gland.^{10,11}

The normal range for total calcium, about 8.6-10.2 mg/dl (2.15-2.54 mmol/l). Normal values and reference ranges may vary among laboratories as much as 0.5 mg/dl.¹² About 50% of total serum calcium is in ionized form, 40% is albumin-bound and 10% is complexed to phosphate or citrate.⁹ The physiologically and clinically important fraction of the serum total calcium is the ionized calcium.¹³ But it is costly and facility is not available everywhere. Almost all laboratories, only total calcium is routinely measured, and ionized calcium concentration is calculated based on calcium, protein or albumin concentrations for many plasma samples.¹⁴

Adjusted calcium = calcium - albumin + 4 · 0, where calcium is in mg/100 ml and albumin in g/100 ml.¹⁵ Another formula also used corrected calcium (mg/dl) = total calcium (mg/dl) + 0.8 × [4 – serum albumin (g/dl)].¹⁶

Hypocalcemia is a clinical situation where there is an electrolyte imbalance is noted with a low serum calcium level which may or may not produce clinical symptoms. There are different studies that use different cut off values for low serum calcium level for

defining hypocalcemia.¹⁷ So incidence of hypocalcemia differs from study to study.

When calcium level falls below the normal range it does not produce clinical symptoms. Only one third of the biochemical hypocalcemia produces symptoms. Most common symptoms of hypocalcemia are paresthesia, muscle spasms, cramps, tetany, circumoral numbness, and seizures. Hypocalcemia can also present with laryngospasm, neuromuscular irritability, cognitive impairment, personality disturbances, prolonged QT intervals, electrocardiographic changes that mimic myocardial infarction, or heart failure.¹⁸⁻²⁰

Now-a-days paradigm of surgical practice is being shifted to day care and outpatient procedures. Total thyroidectomy is also being performed as a short-stay or even an outpatient procedure.²¹ Evidence based parameters are needed to define which patients are eligible to undergo outpatient total thyroidectomy safely.²² For this, preoperative prediction of complications of total thyroidectomy can help to define this criteria.^{23,24}

Early detection of hypocalcemia is crucial for its management. So early prediction of hypocalcemia can make the thyroid surgeons more confident in management of these patients.

This study has evaluated the frequency of hypocalcemia after total thyroidectomy. Associated risk factors for the development of hypocalcemia were also tried to be found out.

The main objective of this study was to evaluate post-thyroidectomy hypocalcemia in relation to thyroid gland pathology.

Methods:

Operational definition: Hypocalcemia was defined as serum calcium level less than 8.4 mg/dl equivalent to less than 2.1 mol/L

Study procedure: This is a Cross sectional study and was conducted in the department of Otorhinolaryngology-head & neck surgery of Dhaka Medical College hospital from January 2017 to December 2017. All the patients who underwent total thyroidectomy at the department had been considered as the study population. We excluded the patients underwent total thyroidectomy with preoperative hypocalcemia, with neck dissection, due to parathyroid gland pathology, unwilling to comply with study protocol. Following inclusion and exclusion criteria sample was enrolled by consecutive purposive random sampling.

Thyroid gland has been assessed by palpation in all the patients. Detailed history and clinical examination was done to determine any obvious clinical features of malignancy and any feature of thyroid dysfunction are recorded.

FNAC and Ultrasonography of thyroid gland were performed outside the department. Serum calcium, albumin, FT4, TSH concentration has been measured preoperatively. Operation procedure and findings were noted. No oral calcium with/without calcitrol or intravenous calcium gluconate were given unless patients had symptoms. In first postoperative day serum calcium and serum albumin were also measured. Here serum Free T4 was calculated in picomol/liter. (Conversion rate $1\text{pmol/l} = 0.0777\text{ ng/dl}$. $1\text{ng/dl} = 12.872\text{ pmol/l}$.) and TSH was measured in mili IU/L or micro IU/ml. Serum calcium was measured in mg/dl. Payny's formula was used to calculate corrected calcium.

Ethical issues: Ethical clearance for the study was taken from the institutional review board and concern authority of Dhaka Medical College.

Statistical analysis: Statistical package for social science (SPSS) 16.0 for windows (SPSS Inc., IL, USA) was used for statistical analysis. Mean values were calculated for

continuous variables. The quantitative observations were indicted by frequencies and percentages. A P value less than 0.05 ($P < 0.05$) was considered to be statistically significant.

Results:

In this study the mean age 42.47 ± 14.16 years and the range is from 7 to 80 years. (Figure-1) The study has female predominance. 104(82.5%) patients were female and 22(17.5%) patients were male. Male : Female ratio was 1: 4.7

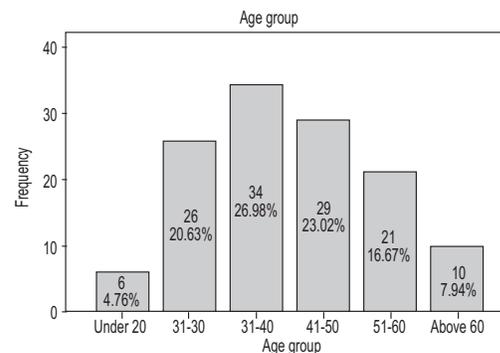


Fig. 1: Bar diagram showing the age distribution of the patients (n=126)

Most of the patient 63 (50%) had multinodular goiter, 37 (29.37%) patients had papillary thyroid carcinoma, 10(7.94%) had follicular thyroid carcinoma and 7(5.56%) had Hashimoto thyroiditis. And 72 (57.1%) had benign thyroid disease and 54 (42.9%) had malignant disease (Table-I).

Table I :

Number of benign and malignant diseases

	Frequency	Percent
Benign	72	57.1
Malignant	54	42.9
Total	126	100.0

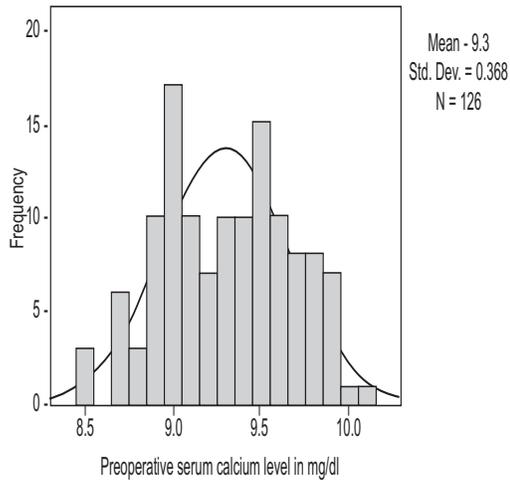


Fig. 2: Histogram showing preoperative serum calcium level

Mean preoperative calcium level was 9.3 mg/dl (+0.360) and the range is from 8.5 mg/dl to 10.2 mg/dl (Figure -2). And mean postoperative calcium level was 8.4 mg/dl (+0.86) and the range is from 6.5 mg/dl to 9.6 mg/dl.

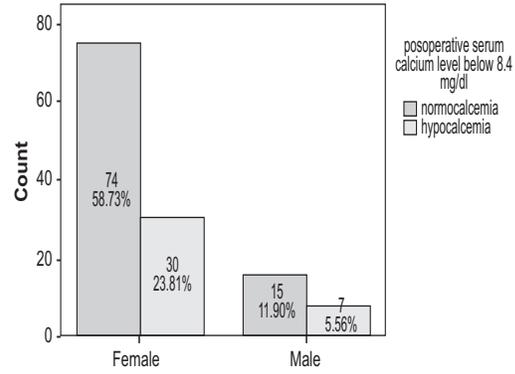


Fig. 4: Bar diagram showing sex distribution of postoperative hypocalcemic patient.

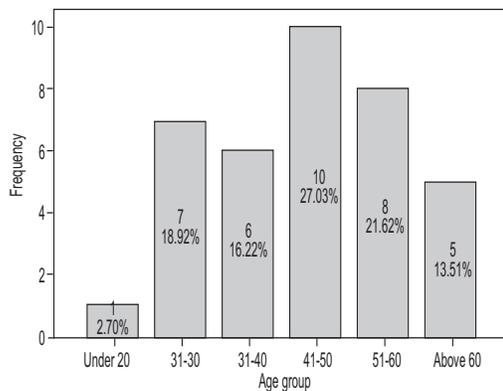


Fig. 3: Bar diagram showing the age distribution of the postoperative hypocalcemic patients (n=37)

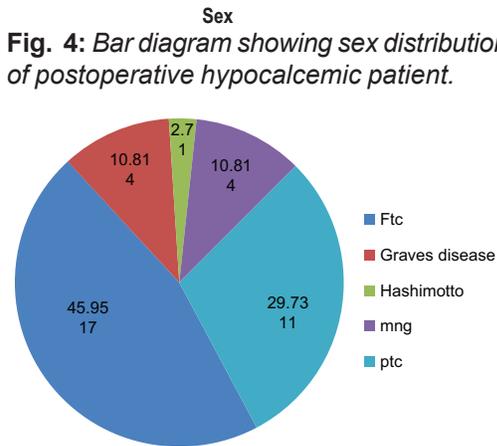


Fig. 5: Pie chart showing different diseases of postoperative hypocalcemia

Table II :
Preoperative and postoperative mean serum calcium level

Different thyroid disease	Mean preoperative serum calcium (mg/dl)	Mean postoperative serum calcium (mg/dl)
Follicular thyroid carcinoma	9.3	8.7
Graves disease	9.5	6.5
Hashimoto thyroiditis	9.3	7.8
Multinodular goiter	9.3	8.7
Papillary thyroid carcinoma	9.3	8.3

Table III :
Comparison of age group in relation with normocalcemia and hypocalcemia.

Age group	Normocalcemia		Hypocalcemia		Total
	Number	Percentage	Number	Percentage	
Under 20	5	84	1	16	6
21-30	19	74	7	26	26
31-40	28	83	6	17	34
41-50	19	66	10	34	29
51-60	13	62	8	38	21
above 60	5	50	5	50	10
Total	89		37		126

Table IV :
Comparison of demographic characteristics and pathological diagnosis of thyroid disease between patients with and without post-operative hypocalcaemia.

Variables	Postoperative hypocalcaemia	
	Normocalcemia (≥ 8.4 mg/dl) 89(70.6%)	Hypocalcaemia (< 8.4 mg/dl) 37 (29.4%)
Age (years) mean (min-max)	43 (7-75)	41 (16-80)
Sex		
Female N (%)	74 (59.5)	30 (23.0)
Male N (%)	15 (11.9)	7 (5.6)
Histopathological diagnosis*		
Benign (%)	56 (44.4)	16 (12.7)
Malignant (%)	33 (26.2)	21 (16.7)

Table V :
Association between pathological diagnosis of thyroid disease and postoperative hypocalcaemia.

Variables	Postoperative hypocalcaemia	P-value ^o
Histopathological diagnosis	95%CI	
Benign (%)	Reference	
Malignant (%)	2.10 (0.94-4.70)	0.072

* Statistically significant at two sided P-value < 0.05 .

^o Association between pathological diagnosis of thyroid disease and post-operative hypocalcaemia adjusted for age and sex (n=126).

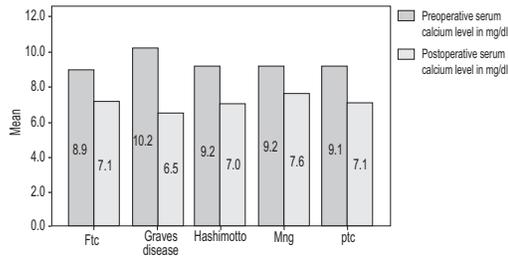


Fig. 6: Bar diagram showing comparison between pre & postoperative serum calcium in hypocalcemic patient (n=37)

Discussion:

Among the complications of thyroid surgery postoperative hypocalcemia is one of the most common complication that is considered for outcome audit.²⁵ If this hypocalcemia persists it significantly reduces the quality of life and is associated with various deleterious effects on general health.²⁶

Hypocalcemia can be classified in different ways like transient and permanent, biochemical and clinical. In our study we included all the transient and biochemical hypocalcemia cases. Permanent or persistent hypocalcemia is defined if hypocalcemia persists even after six month of thyroid surgery.²⁷ The symptoms of hypocalcemia usually manifest 24 to 48 hours after surgery.²⁸ Symptoms are muscle cramps, perioral and peripheral paresthesias, carpopedal spasm or tetany and confusion. Signs of hypocalcemia are the Chvostek's sign and the Trousseau's sign.²⁶ Only one-third of patients who developed biochemical hypocalcemia required treatment.¹⁷

To do work with postoperative hypocalcemia first it difficult to define hypocalcemia. Normal range of any biochemical in human body usually includes mean and two standard deviations above and two standard deviation

below. Usually its range for calcium is 8.6-10.2mg/dl.¹⁶

In different study cut off level for hypocalcemia was defined differently. Shaha and Jaffe in their study used hypocalcemia for the patient having serum calcium less than 2.1mmol/L during their first week follow-up after thyroidectomy.²⁹ Adjusted Serum Ca less than 2.0 mmol/l was calculated for hypocalcemia by Rix TE, Sinha P. in their study of Inadvertent parathyroid excision during thyroid surgery.³⁰ Ku CF et al. defined Hypocalcemia when S Ca < 1.7 mmol/L or symptoms develop calculated for total and sub-total thyroidectomies.³¹

In our study we defined hypocalcemia if the postoperative serum calcium was less than 8.4 mg/dl or 2.1 mmol/L and that is recommended by The British association of endocrine and thyroid surgeons, fifth national audit report.³²

Factors that affect hypocalcemia can be classified into different groups- biochemical, surgical, patient and disease related.³³ Biochemical factors are measured preoperatively and they are- serum calcium, parathyroid hormone, vitamin D, Magnesium, alkaline phosphatase. Surgery related factors are peroperative findings and they are- parathyroid identification, in situ preservation of parathyroid glands, parathyroid auto-transplantation, central neck dissection, inadvertent parathyroidectomy, surgical volume and duration, re-operative surgery. Patient factors are- age at surgery, gender, Disease related factors i.e- Graves' disease, weight of excised specimen, retrosternal extension.³³ In our study we only searched for the disease related factors that may affect the postoperative hypocalcemia.

Pradeep et al. identified low preoperative serum calcium is a predictive factor for

postoperative hypocalcemia after total thyroidectomy.³⁴ In our study it is also found the same result. But in that study Pradeep et al. found age was not significant in postoperative hypocalcemia. In our study older age group developed more hypocalcemia ($p < 0.006$). Which is similar to the finding of Sousa et al.³⁵ No significant difference was noted in their study and it is same in our study.

The literature shows conflicting data regarding postoperative hypocalcemia after total thyroidectomy and gender. Lombardi et al.³⁶ and Scurry et al.³⁷ demonstrated no interference of gender postoperative hypocalcemia. In contrast, other authors^{38,39} showed women had higher incidence of postoperative hypocalcemia. We found no relation between gender and postoperative hypocalcemia ($p < 0.907$).

In our study we found that hypocalcemia is more frequent in the malignant disease than the benign ($p < 0.009$), which is similar to the findings of Sousa et al.³⁹ But in multivariate analysis relationship with thyroid pathology and postoperative hypocalcemia is very close to significance ($p < 0.072$). We could overcome this if the study would conducted with larger sample size. In our finding malignant pathology causes more postoperative hypocalcemia which might be due to some surgery related factors.

Conclusion:

The incidence of postoperative hypocalcemia following total thyroidectomy is 29.4% that is higher than the anticipated but is comparable to other published series. For total thyroidectomy surgeons should be aware of postoperative hypocalcemia but prophylactic calcium and vitamin D supplement is not mandatory in all cases. We can recommend routine postoperative calcium supplementation in elderly and malignant cases and the patient with low

preoperative serum calcium and in these cases serum calcium should be done postoperatively.

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