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Incidence of Hypocalcemia Post Total Thyroidectomy

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Abstract

In the modern era, total thyroidectomy is being performed as a short-stay procedure. Hypocalcemia is the most common complication post total thyroidectomy. It is a major post-operative complication, causing severe symptoms and increasing hospitalization time. Evaluated the incidence of hypocalcemia in patients after total thyroidectomy. A total of 50 patients presented with thyroid disease in Al-Zahraa University Hospital from January 2022 to December 2022. The overall age range was from 20 to 60 years, and the majority of the patients were females 82%. All selected patients underwent total thyroidectomy for benign and malignant thyroid diseases and followed up by postoperative measurement of serum calcium level and clinical assessment for symptoms and signs of hypocalcemia. In this study post-operative hypocalcemia developed in 12 patients, about 24% of study group (50 patients); 8 patients developed asymptomatic hypocalcemia about 16% of all patients or 66.7% of hypocalcemic patients, while 4 patients developed symptomatic hypocalcemia about 8% of all patients or 33.3% of hypocalcemic patients. The mean of calcium level was pre-operatively 9.38±0.32 and postoperatively 6.76±0.38 and 6.64±0.36 after 24 hours and 48 hours respectively in post-operatively hypocalcemic patients (N=12). In female patients' postoperative hypocalcemia developed in 26.8% (11/41) of cases, while in male patients it developed in 11.1% (1/9) of cases. incidence of postoperative hypocalcemia 16.6%, 22.2%, 23.5% & 27.8% in 4 age groups; patients aged from 20 to 30, from 30 to 40, from 40 to 50 and from 50 to 60 years respectively. The incidence of postoperative hypocalcemia was 12.9% for benign MNG, 44.4% for malignant thyroid disease, 42.9% for controlled toxic goiter and 33.3% for Hashimoto's thyroiditis. The incidence of post-operative hypocalcemia was 50%, 45.5%, 16.7% and 15.4% in the groups where the number of parathyroid glands identified in each case was 1 gland, 2 glands, 3 glands and 4 glands respectively. This study demonstrates the incidence of post total thyroidectomy hypocalcemia to be about 24%. The majority of cases developed asymptomatic hypocalcemia and needed no treatment or only oral administration of Ca and vitamin D preparations. There was no permanent hypocalcemia. There is a number of different patients (gender), disease related (etiology of thyroidectomy) and surgical (number of parathyroid glands identified during surgery) risk factors that may be predictive of the development of hypocalcemia following total thyroidectomy that we observed. However, these variables and others should be assessed thoroughly to be taken into account when decisions are being made about how to most effectively prevent or manage hypocalcemia post total thyroidectomy.

Keywords: Total thyroidectomy, Hypocalcemia, Thyroid disease, Parathyroid

1. Introduction

The thyroid gland is located anterior to the trachea in the muscular triangle. The isthmus is flanked by wing-shaped left and right lobes. Each of the thyroid lobes are embedded with parathyroid glands primarily on their posterior surfaces [1].

The thyroid gland is one of the main regulators of metabolism as it secretes T3 and T4 which typically act via nuclear receptors in target tissues and initiate a variety of metabolic pathways [2].

The parathyroid gland secretes parathyroid hormone (PTH) which regulates calcium and phosphate. PTH effects are present in the bones, kidneys, and small intestines [3].

Total thyroidectomy is surgical removal of all of the thyroid gland may be performed for clinical indications that include multinodular goiter, malignancy, benign nodules or cysts, suspicious findings on fine needle aspiration biopsy, dysphagia from cervical esophageal compression or dyspnea from airway compression [4].

The advantage of surgery is the significant goiter reduction with prompt relief of symptoms and definite tissue diagnosis, but problems have to be taken into account [5].

Two classical complications specific to thyroidectomy arise due to the close anatomic proximity of the thyroid gland with the recurrent laryngeal nerves (RLN) and with the parathyroid glands. Postoperative compressive hematoma with acute dyspnea is a rare but severe complication that may result in death or severe long-term sequelae [6].

Hypocalcemia remains one of the major post-operative complications of total thyroidectomy causing potentially severe symptoms and anxiety in affected patients and increasing hospitalization time. Transient hypocalcemia often observed after the operation generally responds favourably to replacement therapy within a few days or weeks [7].

The primary cause of hypocalcemia is secondary hypoparathyroidism following damage to or devascularisation of one or more parathyroid glands during surgery. Erroneous parathyroid removal may also be responsible [8].

Risk factors for post-operative hypocalcemia following total thyroidectomy include thyroid gland size, retrosternal extension of the thyroid, type of thyroid disorder, extent of surgery and whether re-operation is necessary [9].

Hypocalcemia can be asymptomatic particularly if calcium levels are only mildly reduced or symptomatic with muscle spasms and paresthaesia. Severe neurological manifestations may occur if the condition is not adequately treated [10].

Post-operative hypocalcemia may require calcium and Vitamin D supplementation with monitoring until blood calcium returns to normal thus hospitalisation is typically prolonged [11].

The Aim of this work was evaluated the incidence of hypocalcemia post total thyroidectomy.

2. Patients and Methods

This study is an observational, analytical cohort study to evaluate the incidence of hypocalcemia in 50 patients that undergo total thyroidectomy in Al-Zahraa University Hospital from January 2022 to December 2022.

2.1 Ethical Considerations:

This study was conducted according to the standards approved by the Al- Azhar University's Research Ethics Committee. All participants signed the informed consent after full explanation of the study details.

2.2 Inclusion criteria:

- Benign multinodular goiter
- Malignant thyroid disease
- Controlled toxic goiter
- Hashimoto's thyroiditis
- Preoperative normal serum calcium level
- Virgin neck
- Total thyroidectomy

2.3 Exclusion criteria:

- Solitary thyroid nodule
- Recurrent goiter
- Preoperative serum calcium level below 8.5 mg/dl
- Hemithyroidectomy
- Patients unfit for surgery

2.4 Methodology:

All selected patients presented with thyroid disease from age 20 years old to 60 years old which were diagnosed by complete history taking including personal history (age, sex, residence and special habits), complaint (neck swelling), present history (onset, course, duration of the thyroid disease, associated disorders, history of medications), past history of any general or local disease, examination (general and local) general to detect signs of systemic diseases and local examination of the neck. Preoperative measurement of serum calcium level and thyroid function and neck ultrasound. FNAC was done for suspicious cases by ultrasound.

A total of 50 patients were available for the study:

- The overall age ranges from 20 to 60 years (N= 50).
- The majority of the patients were females 82%
- All patients presented with neck swelling (either painless or painful),
- and assessed pressure symptoms and symptoms of thyrotoxicosis or hypothyroidism which was not present.
- All patients had normal serum calcium level preoperatively
- These patients were evaluated using flexible laryngoscopy to assess the vocal cords. The examination was negative for vocal cord paralysis in all patients.

All selected patients underwent total thyroidectomy with identification of parathyroid glands.

All patients were followed up by postoperative measurement of serum calcium level: at 24 hours, 48 hours and 6 months postoperatively; and clinical assessment for symptoms and signs of hypocalcemia.

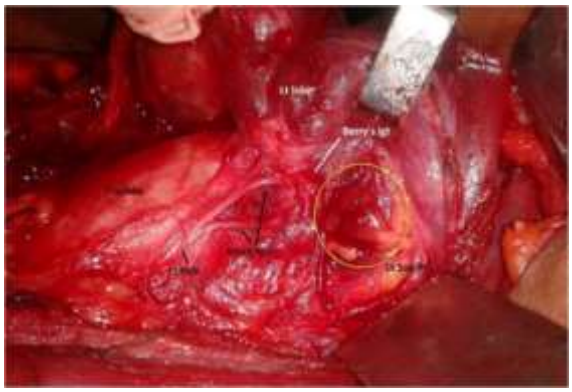

Figure (1): Left superior parathyroid gland and Recurrent Laryngeal nerve (RLN) **(12)**

Figure (2): recurrent laryngeal nerve and parathyroid gland

2.5 Statistical analysis:

Data analysis was performed using SPSS version 24.0 and MS Excel 2016. Univariate descriptive statistics were performed for the continuous data. Categorical data were summarized as frequencies and percentages. The chi-square test or the Fishers exact test was used to estimate the associations between categorical variables. Level of statistical significance was determined at $p < 0.05$.

3. Results

As show in table 1 A total of 50 patients (41 women and 9 men) underwent total thyroidectomy over the study period. Patient age ranged from 20 to 60 years with a median age of 40 years.

As shown in table 2 this diagnosis was according to symptoms, signs, preoperative laboratory investigations, neck ultrasound and FNAC and postoperative histopathological confirmation

Table 1: Demographic data of the patients studied:

Demographic Data		
Gender	No.	%
Female	41	82
Male	9	18
Total	50	100
Age (Range in years)		
20 – 30 Y	6	12
30 – 40 Y	9	18
40 – 50 Y	17	34
50 – 60 Y	18	36
Mean±SD	44.14 ± 9.80	

Table 2: Etiology of thyroid diseases distribution of the study group

Etiology of Thyroidectomy	No.	%
Benign multinodular goiter	31	62
Malignant thyroid disease	9	18
Controlled toxic goiter	7	14
Hashimoto's thyroiditis	3	6
Total	50	100

Table 3: Distribution of patients with postoperative normocalcemia, symptomatic and asymptomatic hypocalcem

	No.	%
Normocalcemic patients	38	76
Hypocalcemic patients	12	24
Symptomatic hypocalcemia	4	8
Asymptomatic hypocalcemia	8	16
Total number of patients	50	100

Table 4: Demographic distribution of patients who developed hypocalcemia according to age and se

	Hypo-calcemic (N=12)	Normo-calcemic (N=38)	% of Hypo-calcemic	P- value	Significance
Gender					
Female (N=41)	11	30	26.8%	0.001	Significant (S.)
Male (N=9)	1	8	11.1%		
Age					
20–30 Y (N=6)	1	5	16.6%	0.207	Not significant (N.S.)
30–40 Y (N=9)	2	7	22.2%		
40–50 Y (N=17)	4	13	23.5%		
50–60 Y (N=18)	5	13	27.8%		

Table 5: Histopathological diagnosis of the patients underwent this study. In regarding the transient hypocalcemia

	Hypo-calcemic (N=12)	Normo-calcemic (N=38)	% of hypo-calcemic	P-value	Significance
Benign multinodular goiter (N=31)	4	27	12.9	0.311	N.S.
Malignant thyroid disease(N=9)	4	5	44.4	0.126	N.S.
Controlled toxic goiter (N=7)	3	4	42.9	0.797	N.S.
Hashimoto's Thyroiditis (N=3)	1	2	33.3	0.572	N.S.
Total number of patients (N=50)	12	38	24		

Table 6: Total number of parathyroid glands identified during operation in hypocalcemic group:

No. of identified glands	Hypo-calcemic (N=12)	Normo-calcemic (N=38)	% of hypo-calcemic	P- value	Significance
1 gland (N=2)	1	1	50%	< 0.001	S.
2 glands (N=11)	5	6	45.5%		
3 glands (N=24)	4	20	16.7%		
4 glands (N=13)	2	11	15.4%		

4. Discussion

Hypocalcemia is a common complication after total thyroidectomy. It usually occurs in first days after surgery, and it can be symptomatic or asymptomatic. The frequency of transient hypoparathyroidism after thyroid surgery is between 6.9 and 49% [13].

In this study A total of 50 patients underwent total thyroidectomy over the study period from January 2022 to December 2022, Patient age ranged from 20 to 60 years with a median age of 40 years and females represented the majority of the study (82%); the etiology of thyroid diseases in this study was benign multinodular goiter (62%), malignant thyroid disease (18%), controlled toxic goiter (14%) and Hashimoto's thyroiditis (6%), according to symptoms, signs, preoperative laboratory investigations, neck ultrasound and FNAC and postoperative histopathological confirmation.

In this study post-operative hypocalcemia developed in 12 patients, about 24% of study group (50 patients). The majority of cases developed asymptomatic hypocalcemia and needed no treatment or only oral administration of Ca and vitamin D preparations. In this study 8 patients developed asymptomatic hypocalcemia about 16% of all patients or 66.7% of hypocalcemic patients. While 4 patient developed symptomatic hypocalcemia about 8% of all patients or 33.3% of hypocalcemic patients. We found that the mean of calcium level was pre-operatively 9.38±0.32 and postoperatively 6.76±0.38 and 6.64±0.36 after 24 hours and 48 hours respectively in post-operatively hypocalcemic patients (N=12). The decreased calcium levels slowly increased and returned to normal values. However, the recovery rate of serum calcium levels was increased based on the causality of the pathology. There is no permanent hypocalcemia. Transient hypocalcemia was treated, and the results were normal in a 6-month period for all the subjects of the study.

In a study performed by Nair et al., with 806 patients the overall incidence of hypocalcaemia was 23.6% and Symptomatic hypocalcaemia occurred in 10.91% patients [14]. In a study by Del Rio et al. performed on 2108 patients with 37.7% patients developed early post-operative hypocalcemia [13]. In a multicenter study with 14,934 patients, Rosato et al. found that 10% of patients had symptomatic hypocalcemia. However, that study included patients who had TT (64.3%) and smaller-scale surgeries on the thyroid (35.7%) [15].

In this study female patients experienced postoperative hypocalcemia in 26.8% (11/41) of cases, while the males showed lower incidence of postoperative hypocalcemia with 11.1% incidence detected in men. So females seemed to be more prone to develop postoperative hypocalcemia.

As regard to sex, in some studies sex has not been shown to affect calcium homeostasis postoperatively [16]. Other studies reports that female sex is associated with a significantly higher incidence of hypocalcemia compared with males [17].

Many studies tried to find an explanation to female predisposition to post-thyroidectomy hypocalcemia, but the specific mechanisms underlying this gender difference can only be assumed. The gender disparity may be related to effects of sex steroids on PTH secretion, genetic variation among cell-signaling pathways or anatomic differences that can cause more frequent iatrogenic damages because of a more diminutive operative field [18].

In this study we divided patients into 4 age groups; patients aged from 20 to 30, from 30 to 40, from 40 to 50 and from 50 to 60 years with incidence of postoperative hypocalcemia 16.6%, 22.2%, 23.5% & 27.8% respectively. Therefore, there was

no significant intergroup difference as regard to patient age.

There are many opinions regarding correlation between development of postoperative hypocalcemia and patient age. Some studies found transient hypocalcemia to be associated with advanced age [19], whereas others reported an association with younger age [20]. A systematic review performed by Edafe et al. observed no significant difference in mean age between patients who had transient hypocalcemia and those who did not [17].

In this study, the incidence of postoperative hypocalcemia was 12.9% for benign MNG, 44.4% for malignant thyroid disease, 42.9% for controlled toxic goiter and 33.3% for Hashimoto's thyroiditis. There was decreased incidence of postoperative hypocalcemia in benign MNG compared to other etiologies in this study.

Some studies showed that thyroidectomy for carcinoma has a higher risk for hypocalcemia because in case of malignant pathology posterior capsule is radically removed with the gland and this is the reason why parathyroid glands are at higher risk of injury [21]. While others found that surgery for malignant pathology was not found as a significant factor for the development of post thyroidectomy hypocalcemia [22].

In other studies, hyperthyroidismis described as a risk factor for early hypocalcemia development; it is unclear why thyrotoxic thyroidectomies have an increased rate of hypocalcemia; however, it is perhaps unsurprising as the thyroid gland in thyrotoxicosis tends to be larger than normal and very highly vascularized leading to a more challenging operation [23]. While in a study by Del Rio et al., thyroid hyperfuntion didn't appear as a significant factor in early hypocalcemia development [13].

In a study by Nair et al., hypocalcaemia was significantly high in a small subset of classic Hashimoto thyroiditis [14]. While in astudy by Shih et al., the incidence of hypocalcemia was 4.4% in hashimoto's thyroiditis [24].

In this study the number of parathyroid glands identified in each case was 1 gland in 2 patients, 2 glands in 11 patients, 3 glands in 24 patients and 4 glands in 13 patients. The incidence of post-operative hypocalcemia was 50%, 45.5%, 16.7% and 15.4% in each group respectively. This data shows the increasing rate of hypocalcemia with decreased number of identified glands.

In a study by Eismontas et al, it stated that the greater the number of PGs found during surgery, the lower the chance of hypocalcemia [25]. In a study by Thomusch et al, it determined that permanent post-operative hypocalcemia was more likely to develop if less than two PGs were found during surgery [26]. In a study by Praženica et al. stated that identification of a higher number of parathyroid glands is associated with a higher incidence of postoperative temporary hypocalcemia and permanent hypoparathyroidism [27].

To avoid potential injury to the parathyroid glands, every surgeon must be thoroughly aware of their anatomic complexity that contributes to difficulty of identification and possible injury. Strict adherence to capsular dissection represents the optimum method for safe preservation of parathyroid glands without necessitating their systemic identification. Distal ligation of all terminal branches of the superior and inferior thyroid arteries, close to the thyroid capsule, enables reliable separation of all tissues carrying parathyroid gland away from the thyroid surface. Continued dissection in this tissue, with the aim to identify all parathyroid glands may increase the risk of their mechanical injury or devascularization according to some studies [13].

5. Conclusion

The findings of this study suggests that gender, the etiology of thyroidectomy and

identification of parathyroid glands during surgery are factors affecting the development of hypocalcemia post total thyroidectomy; with female sex showing higher incidence of hypocalcemia, while decreased incidence of hypocalcemia with identification of parathyroid glands during surgery and with benign multinodular goiter. While age was not a significant factor in the development of hypocalcemia. However, these variables and others should be assessed thoroughly to be taken into account when decisions are being made about how to most effectively prevent or manage postoperative hypocalcemia after total thyroidectomy.

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