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Multivariate Analysis of Factors Associated with and Predicting Post-Thyroidectomy Hypoglycaemia: Experience of the Surgery a Department at Ibn Sina Hospital

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Post-thyroidectomy hypocalcaemia continues to be a regular complication. Therefore, it is necessary to identify predictive factors to improve preoperative risk assessment and reduce complications.
Materials and Methods: This retrospective study was performed at the Surgical Department A of Ibn Sina Hospital from 2007 to 2022 and analyzed 539 thyroidectomy cases. The objective is to ascertain the factors that contribute to postoperative hypocalcaemia, whether it is transient or permanent. Parameters consist of age, gender, past medical history, preoperative symptoms,

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thyroid hormone levels, diagnosis, surgical procedure type, detection of parathyroid gland, incidentaloma, lymph node dissection, and operator proficiency.
Results: The findings reveal that postoperative hypocalcaemia occurred in 31.91% of patients, 6.39% of whom necessitated extended calcium supplementation. Significant factors associated with the condition included being female, having preoperative hyperthyroidism, undergoing total thyroidectomy, experiencing accidental parathyroidectomy, and having a multinodular goiter.
Presence, or lack thereof, of parathyroid glands, parathyroid incidentaloma, surgical expertise, and incidents of hematoma or hemorrhaged requiring revision surgery were also significant factors.
Conclusion: There was no statistically significant impact from surgical history, hypertension, or diabetes. Understanding these predictive factors is essential to improve surgical strategies, optimize patient care, and potentially reduce hospitalization costs associated with post-thyroidectomy hypocalcemia. Further research should investigate the interaction between these factors and refine risk prediction models to enhance patient outcomes.

Keywords: Prevention; thyroidectomy; hypocalcemia; thyroid surgery.

1. **INTRODUCTION**

Hypocalcaemia can occur after thyroidectomy due to devascularisation or accidental removal of the parathyroid glands during the procedure, as they secrete parathyroid hormone, which helps to regulate blood calcium levels [1].

Although post-thyroidectomy hypocalcemia can be severe, it is often reversible. However, it can be brief or everlasting and can result in expensive hospitalization charges if calcium supplementation is required. Hypocalcaemia tetany is the most common complication of thyroidectomy and can range from mild symptoms to serious complications. symptoms to serious complications that may be asymptomatic or symptomatic. [2].

Many endocrine surgeons aim to predict hypocalcaemia at an early stage to prevent serious complications and initiate treatment to reduce the length of hospital stay.

This retrospective observational study aims to prevent or develop a better management strategy for hypocalcaemia in patients undergoing different types of thyroidectomy for different pathologies, based on factors that may predict postoperative, transient or permanent hypocalcaemia.

The objective of this article is to analyse the factors linked to post-thyroidectomy hypoglycaemia in our department, in order to enhance our therapeutic procedures.

2. METHODOLOGY

We conducted a retrospective study using available medical records and computerised data covering the period January 2007-December 2022, including patients who underwent thyroid surgery for various thyroid pathologies at Ibn Sina Hospital's "A" Surgery Department.

Patients with concomitant parathyroid disease and renal failure were excluded from this study.

The parameters studied included age, sex, medical history, previous thyroid surgery, preoperative symptoms, preoperative TSH levels, diagnosis, type of surgery, identification of parathyroid glands during surgery, incidental discovery of parathyroid glands, type of lymph node dissection, and surgeon expertise.

The postoperative hypocalcemia group was linked with the various parameters examined to identify those that had statistical significance.

Qualitative variables are illustrated by frequencies and percentages. We calculated differences in frequencies between groups using either Fisher's exact test or the CHI 2. Statistical significance of the various factors was also calculated. We considered odds ratios, 95% CIs, and a p-value less than 0.05 to be indicative of statistical significance.

3. RESULTS

The records of 539 patients undergoing thyroid surgery for different thyroid pathology in the "A" surgery department of the Ibn Sina Hospital, Rabat, from January 2007 to December2022, and meeting our inclusion criteria, were collected.

Factors associated with postoperative hypocalcemia included age, sex, medical and surgical history, preoperative symptoms, preoperative TSH level, diagnosis, type of surgery, identification of parathyroid glands during surgery, detection of parathyroid incidentaloma, type of lymph node dissection, and surgeon skill.

In our study, 172 patients (31.91%) had postoperative hypocalcaemia (<80 mg/dl). 11 patients had permanent hypocalcaemia requiring unrestricted calcium supplementation.

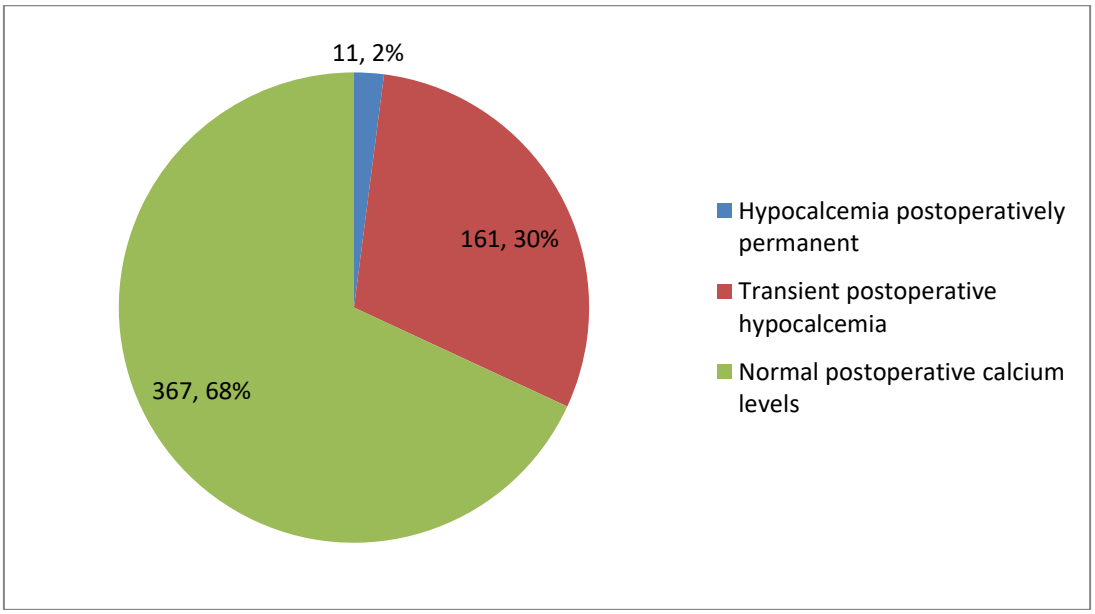

Fig. 1. Distribution of Postoperative Calcium Levels

- **Age:**

The mean age of the patients who developed post-operative hypocalcaemia was 46.31 ± 13.7 years, compared with 47.7 ± 14.6 years for the patients who didn't develop hypocalcaemia, with a p-value of 0.477. Furthermore, in our study we found that 161 female patients (33.40%) compared to 11 male patients (19.29%) developed postoperative hypocalcaemia. The odds ratio was 0.48, CI [0.24-0.95] and the p-value was 0.031.

- Previous thyroid-related surgery: In our study, we found that 19 patients (24.67%) who had previously undergone thyroidectomy experienced postoperative hypocalcaemia, compared with 153 patients (33.11%) who underwent first-time thyroidectomy, although the difference was not statistically significant (p=0.14). Among those affected, 18 patients (23.37%) recovered soon after the procedure, while 1 patient (1.29%) experienced permanent hypocalcemia.
- We also found that 22 of the patients (24.71%) with postoperative hypocalcaemia had a history of hypertension compared to 150 (33.33%) without, but again the difference was not statistically significant (p=0.11). Hypocalcaemia was temporary in 21 patients (23.59%), with a non-significant p-value of 0.15. However, only one patient (1.12%) had permanent hypocalcaemia. The p-value was 0.50.

- **Diabetes:**

Of 172 patients with postoperative hypocalcaemia, only 13 (27.08%) were diabetic. 159 (0.32%) were not (p=0.45). The 13 patients with hypocalcaemia had transient symptoms (p=0.45) and the diabetics did not have permanent hypocalcaemia (p=0.29).

- **Diagnosis:**

Postoperative hypocalcaemia occurred in 124 patients (35.63%) diagnosed with Multi-Nodular Goitre (MNG) compared to 48 patients (25.13%) with other diagnoses, with a p-value of 0.012.

The condition was transient in 113 patients (32.47%) with a p-value of 0.07 and permanent in 11 patients (3.16%).

Permanent hypocalcaemia did not develop in any of the patients with other diagnoses, with a p-value of 0.013.

Transient hypocalcemia was observed in 143 symptomatic patients (32.72%) with p=0.003 versus 9 cases of permanent hypocalcemia (2.05%) with p=0.94.

- **TSHus :**

Of the 172 patients who developed post-thyroidectomy hypocalcemia, 64 (36.15%) had preoperative hyperthyroidism compared with 108 patients (29.83%) with normal TSH levels, with p<0.001.

Transient hypocalcemia was observed in 61 patients (34.46%) with p<0.001. It was permanent in 3 patients (1.69%) with p=0.13.

- **Type of intervention :**

Two patients (3.57%) developed postoperative hypocalcemia after isthmolobectomy, compared with 170 patients (35.19%) in the second group who had bilateral surgery, p<0.001.

Table 1. Presence of pre-operative symptoms

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Pre-operative symptoms	152	285	437		
No pre-operative symptoms	20	82	191		
Total	172	367	539	8,76	0,003

Table 2. Transient hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Pre-operative hyperthyroidism	64	3	67		
TSH normal	108	364	472		
Total	172	367	539	142,49	< 0,001

Table 3. Parathyroid incidentaloma

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Parathyroid incidentaloma	4	1	5		
No parathyroid incidentaloma	168	366	534		
Total	172	367	539	5,37	0,02

Among patients who underwent total thyroidectomy, it was transient in 159 (32.92%) and permanent in 11 (2.27%) with p<0.001.

None of the patients who underwent isthmolobectomy developed permanent hypocalcemia, with p = 0.25.

- **Detection of parathyroid glands :**

In our study, 481 patients (89.23%) underwent total thyroidectomy. Of the 445 patients who had more than 2 parathyroid glands seen during the operation, 158 (35.50%) developed postoperative hypocalcemia versus 12 patients (35.29%) of the 34 patients who had less than 2 parathyroid glands seen during the operation, with p<0.001.

Of the 56 patients (10.38%) who underwent isthmolobectomy, 1 patient (2.38%) out of the 42 in whom both parathyroid glands were seen, developed hypocalcemia versus 1 patient (9.09%) out of the 11 patients who had only 1 parathyroid gland seen during surgery, with p = 0.4.

- **Parathyroid incidentaloma:**

Among patients with postoperative hypocalcemia, 4 (80%) had a parathyroid incidentaloma out of the 5 incidentalomas, compared with 168 (31.46%) out of 534 without incidentaloma, with p=0.02.

After unintentional parathyroidectomy and of parathyroid glands, post-operative hypocalcemia was observed in 42.86% of the 18 patients who underwent the procedure compared to 30.98% of the 154 patients who did not.

Post-operative hypocalcaemia was observed in 42.50% of the 40 patients who received parathyroid autograft compared with 31.06% of the 155 patients who did not receive parathyroid autograft, but this difference was not statistically significant (p = 0.11). Transient hypocalcemia was noted in both groups.

- **Surgical expertise:**

Of the 51 surgical procedures performed by residents, 10 (19.60%) developed postoperative hypocalcemia, compared with 162 patients (33.19%) operated on by senior surgeons (p=0.048).

4. DISCUSSION

In this study, significant variables were female sex, preoperative hyperthyroidism and hypocalcemia, total thyroidectomy, inadvertent parathyroidectomy, multinodular goiter, preoperative hyperthyroidism, number of parathyroid glands detected, parathyroid incidentalomas, surgical expertise, and haematoma or bleeding.

Conversely, the variables that were significant in other studies did not yield significant results in ours. The following factors were identified: advanced age, Graves' disease, thyroid cancer, previous cervical dissection, and size of the thyroid gland.

Our investigation demonstrated that hypertension and diabetes were not considered significant variables.

Potential risk factors for hypocalcaemia after thyroidectomy have been investigated in several studies.

Some of these risk factors have been widely accepted, but the identification of these risk factors remains a challenge. In our research, we analyzed the biological, clinical, and surgical factors that could impact the occurrence of post-thyroidectomy hypocalcemia.

The audit by the British Association of Endocrine and Thyroid Surgeons [3] revealed that rates were 27.4% and 12.1%. There is inconsistent reporting of postoperative hypocalcaemia rates across studies, owing to a lack of agreement on the definition and criteria for the condition [4].

Type : In this case series, we divided our patients into two groups according to procedure: group 1 included patients undergoing isthmolobectomy and group 2 patients undergoing total thyroidectomy.

Our findings show that the rate of post-operative and transient hypocalcemia was significantly higher in the patients who had undergone total thyroidectomy in group 2 ($p<0.001$).

This may seem obvious. In an isthmolobectomy, one side is explored and only two parathyroid glands are exposed, leaving the contralateral lobe intact. It is well known that only one functioning gland is able to maintain a normal calcium metabolism [18].

- **Dissection:**

This study found that central cervical dissection and lateral cervical dissection (LCC) were not significant ($p=0.28$) in the development of post-thyroidectomy hypocalcaemia. However, the extent of anterior cervical dissection had a significant effect ($p=0.038$).

Patients undergoing total thyroidectomy were more likely to experience transient postoperative hypocalcaemia than those undergoing isthmolobectomy.

It seems unlikely that LCC has any effect on the development of hypoparathyroidism, given the general anatomy and location of the parathyroid glands. The degree of LCC was found to be as significant as our findings in a study of 1030 patients undergoing total thyroidectomy [19].

- **Identification of parathyroids:**

In our research, identifying the parathyroid glands was significantly linked to the occurrence of temporary or lasting hypocalcemia ($p<0.001$). Nevertheless, patients undergoing bilateral surgery who had fewer than two parathyroid glands detected during surgery experienced a lower prevalence of transient hypocalcemia after thyroidectomy compared to those who had more than two glands observed during surgery (34 versus 445). This is in line with a study of 569 patients that discovered that deploying the extracapsular technique during total thyroidectomy and identifying fewer parathyroid glands in their orthotopic positions not only lessened the chance of temporary and prolonged hypoparathyroidism but also expedited the recovery from prolonged hypoparathyroidism [20]. Certain authors propose that this is due to the danger of injury connected with parathyroid manipulation [21]. However, it remains unclear whether there is a consensus regarding the recommendation to identify and retain parathyroid glands, or regarding the minimum number of glands that should be retained [22]. In a review of 254 patients, the authors propose that precise dissection of the thyroid capsule as near to the thyroid parenchyma as feasible and identification of the paras before ligating the inferior thyroid artery is crucial in preventing harm to the structure and vascularization, as well as unintentional removal with the thyroid lobe [23].

- **Parathyroid incidentaloma**

We identified 5 patients (0.92%) who had a parathyroid incidentaloma detected during their surgery. Of these, 4 (80%) experienced postoperative hypocalcemia with a p-value of 0.02, which was transient in 3 patients (75%) with a p-value of 0.13, and permanent in 1 patient (25%) with a p-value of 0.004. Our results surpass those reported by I. Benabbad et al. in a prospective study, which found an incidence of 1% of primary hyperparathyroidism disclosed by post-thyroidectomy hypocalcemia [24]. Carnaille and colleagues reported an incidence of 0.6% [24;25] in their study, while Hellman et al found a higher incidence of 2% [26]. The most recent study by Abboud et al. reported an incidence of 1.9% [27].

In the absence of significant risk of recurrence, we have decided to perform resection on any parathyroid incidentalomas to mitigate the risks of subsequent operations. This is because incidentally discovered parathyroid hyperplasia could represent a pre-pathological state leading to HPTP [24].

There were no significant differences observed between diabetic and non-diabetic patients with regard to postoperative ($p=0.45$), transient ($p=0.45$), or permanent ($p=0.29$) hypocalcemia. This finding is consistent for patients with or without diabetes. Unfortunately, information regarding the relationship between diabetes and post-thyroidectomy hypocalcemia was not found.

- **Surgical expertise:**

Our study showed a noteworthy variance in postoperative hypocalcemia between procedures performed by senior surgeons and residents ($p = 0.047$). We observed that post-thyroidectomy hypocalcemia was more pronounced in surgeries performed by senior surgeons (33.19% compared to

19.60% for residents). This could stem from the fact that senior surgeons conducted a significantly higher number of procedures than the residents they supervised.

Experience is crucial for surgeons to prevent post-thyroidectomy complications, according to literature. A cross-sectional study performed at multiple centres revealed that patients face a higher chance of enduring permanent complications after thyroidectomy if it is carried out by less experienced or very seasoned surgeons. The study suggests that surgeons aged between 35 and 50 years provide the safest care [25].

5. CONCLUSION

In This retrospective study, undertaken over 16 years at Ibn Sina Hospital in Rabat, Surgery Department "A," scrutinised the outcomes of thyroid surgery. The study revealed various patient-related clinical and surgical risk factors for post-thyroidectomy hypocalcemia. Significant predictors encompass preoperative hyperthyroidism, total thyroidectomy, the number of identified parathyroid glands, preoperative hypocalcemia, and female gender. The findings indicate the need for consistent assessment of preoperative calcium levels in all patients undergoing thyroidectomy and preoperative evaluation of vitamin D levels in women. Supplementation of calcium and vitamin D in patients with risk factors could mitigate post-thyroidectomy hypocalcemia. Ultimately, a proficient lead surgeon and a systematic approach to thyroidectomy could markedly decrease the occurrence of postoperative hypocalcemia.

CONSENT

As per international standards or university standards, respondents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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