The Egyptian Journal of Hospital Medicine (April 2024) Vol. 95, Page 1478- 1482

Incidence and Outcome of Hypocalcaemia after Total Thyroidectomy

Naser A. Zaher, Emad M. Abdelrahman, Atef A. Salem, Mohamed M. Debes, Marwa M. Yosry and Mohamed E. Zayed

General Surgery Department, Faculty of Medicine, Benha University, Egypt

Corresponding Author: Emad M. Abdelrahman**, Email:** emadshan301@gmail.com **Tel: O1226763986, ORCID https://www.orcid.org/0000-0001-6066-2215**

ABSTRACT

Background: Due to its prevalence and the absence of well-established preoperative indicators, hypoparathyroidism poses a significant problem. **Objective:** This study aimed to find characteristics that predict hypocalcemia after total thyroidectomy was the primary goal of this investigation.

Patients and methods: In this prospective analysis, 123 patients who were candidates for a thyroidectomy were enrolled. Early hypocalcemia symptoms and potential risk factors were monitored in these individuals.

Results: The mean age of the studied patients was 47.22 ± 12.2 years. Hypocalcemia was significantly evident in the age group between 40-50 years. Results showed that recurring goiter, Grave's disease, malignant goiter and block neck dissection were significantly correlated with postoperative hypocalcemia.

Conclusion: Malignant goiter, Grave's disease (GD) and recurrent goiter are independent risk factors for post total thyroidectomy hypocalcemia.

Keywords: Goiter, Total thyroidectomy, Hypocalcemia.

INTRODUCTION

Serious significant bleeding and vocal cord palsy, either transient or permanent, are adverse effects that may occur after total thyroidectomy (TT). While thyroid surgery is safe, hypocalcemia is a typical adverse effect [1, 2]. As a therapy for cancer, TT has become more popular in recent decades. Multinodular goitre, GD, and Hashimoto's thyroiditis are among the benign disorders that it is used to treat [3, 4].The parathyroid gland's activity has a direct impact on blood calcium levels [5, 6].

It is possible that the parathyroid gland's location is the primary factor contributing to its destruction. In the loose connective tissue between the true and false capillaries, close to the posterior margin of the thyroid's lateral lobe, are most of the parathyroid glands. When blood flows to the parathyroid gland, it does so via the inferior thyroid artery and anastomosis with the superior thyroid artery. Out of the total number of arteries that supply the thyroid gland, only 80% actually get to the parathyroid gland. Damage to the parathyroid gland may occur as a consequence of vascular spasm caused by careless surgical procedures or clamping the inferior thyroid artery at the thyroid gland's inferior pole [7].

Patients who had thyroid surgery may be complicated by transient hypocalcemia. Hypoparathyroidism, either temporary or permanent can be caused by injury, devascularization, and removal of the parathyroid gland, which results in post-thyroidectomy hypocalcemia. This process may also be influenced by other factors, such as a vitamin D shortage, an abrupt rise in serum calcitonin levels (due to gland manipulation during surgery), or a condition known as "hungry bone syndrome" [8, 9]. Two potential causes that should be considered are hypocalcemia due to dilution and hypocalcemia caused by post-operative alkalosis, which results from hyperventilation due to postoperative pain [10]. Even yet, the most effective way to reduce the risk of postoperative hypocalcemia is to have a thorough understanding of thyroid anatomy with reference to the parathyroid glands' embryonic genesis [11]. The rate of hypocalcemia has declined with the development of parathyroid preservation methods. However the rate of temporary hypocalcemia remains between 6.9 and 49.0% of patients undergoing TT [12, 13].

The ability of a surgeon to anticipate hypocalcemia following a thyroidectomy is crucial for postoperative care. Prompt identification of any potential hypocalcemia risk will shorten hospital stays and minimize pointless testing. Treatment with calcium and vitamin D supplements might delay the start of symptoms [8, 14].

Numerous research with varying conclusions attempted to determine the risk factors of post-TT hypocalcemia (EH). The prevalence of post-operative hypoparathyroidism and the paucity of reliable preoperative predictors continue to provide a clinical dilemma for thyroid surgeons [9]. The grey area about the predictive factors of post TT hypocalcemia, which is why the authors felt compelled to do this research.

PATIENTS AND METHODS

Study design: The current prospective study was conducted throughout the period from January 2020 to November 2023. Eligible patients included in this study were recruited and operated on at Benha University Hospital.

Sample size: This study's primary endpoint, the frequency of postoperative hypocalcemia, was used to determine the sample size. The G power 3.1 program was used to calculate the following: a power of 80%, an effect size of 0.7, a P value of 0.05, and a sample size of 123.

Received: 01/11/2023
Accepted: 05/02/2024

(Universities, Dusseldorf, Germany). The current prospective study included 123 patients eligible for total thyroidectomy. (e.g., Multinodular goiter, GD , malignant thyroid disease).

Exclusion criteria: Patients with preoperative hypercalcemia or hypocalcemia due to any cause as well as patients with renal failure. Patients with neck radiotherapy or those refusing to be included.

All studied cases were subjected to the following: Detailed history taking, examination and investigations including thyroid functions and calcium levels. For all included patients conventional total thyroidectomy was planned with securing the parathyroid glands using classical Kocher collar incision. For patients with preoperative diagnosis of thyroid malignancy eligible for total thyroidectomy and block neck dissection, a more extended J- shaped incision was planned for better exposure and feasible dissection with muscle cutting if needed. If this maneuver is necessary, the muscles should be divided high to preserve their innervation by branches of the Ansa cervicalis.

Postoperative work up: It is standard practice to check for signs of nerve damage after thyroid surgery. Two times daily, beginning on the day of surgery and continuing until the second day after the procedure, symptoms of hypocalcemia were documented, along with their kind. Mild hypocalcaemia was believed to be indicated by symptoms like numbness in the lips or tips of the limbs and positive Chvostek's or Trousseau's signs. Advanced hypocalcaemia was considered to be indicated by symptoms like convulsions, laryngospasm, and carpopedal spasm. Measurements taken after surgery included phosphorus, serum free T3, free T4, total serum hormone, and calcium levels.

Follow up:

- Short-term follow up was hypocalcemia symptoms at day of operation, serum total and ionized calcium levels at post operative day 1. Replacement therapy was delayed till histopathology results.
- Long-term follow up was for 12 months.

Outcome:

- Primary outcome: To be successful at total thyroidectomy with minimal post operative complications especially hypocalcemia.
- Secondary outcome: decreased hospital stay and overall cost.

Ethical Approval: This study was ethically approved by The Institutional Review Board of the Faculty of Medicine, Benha University. Written informed consent was obtained from each participant. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

For statistical analysis, we utilized SPSS, version 25 (IBM Corp., Armonk, New York, USA). Quantitative factors were characterized using means and standard deviations, a Student t test was used. For qualitative indicators that were expressed as a percentage of frequency, the χ^2 test was used. We regarded a p-value $\leq$ 0.05 to be statistically significant.

RESULTS

The current prospective study included 123 patients eligible for total thyroidectomy. The mean age of the included patients was 47.22 ± 1 2.2 years. Nodular goiter was the most common histopathological presentation among benign diseases 74 (72.55%) followed by Grave's disease 14 (13.7%). The malignant lesions presented in 21 (17.1%) of cases. In the current study 19 (15.45%) underwent total thyroidectomy with block neck dissection, while TT was done in 104 (84.55%) (Table (1).

Table (1): Sociodemographic data, histological diagnosis and surgical procedures performed.

variable		No of patients =123 (100%)
Sex		
Female	**N (%)**	**99 (80.5%)**
Male	**N (%)**	**24 (19.5%)**
Age	**Mean ± SD**	**47.22 ± 12.2**
Age groups		
< 40	**N (%)**	**45 (36.6%)**
40-50	**N (%)**	**35 (28.45%)**
50-60	**N (%)**	**29 (23.58%)**
> 60	**N (%)**	**14 (11.37%)**
Co morbidities	**N (%)**	
DM	**N (%)**	**17 (13.8%)**
Hypertension	**N (%)**	**14 ((11.37%)**
IHD	**N (%)**	**4 (3.25%)**
Definitive histological diagnosis		
Malignant	**N (%)**	**21 (17.1%)**
Benign	**N (%)**	**102 (82.9%)**
Graves' Disease	**N (%)**	**14 (13.7%)**
Thyroiditis	**N (%)**	**5 (4.9%)**
Nodular Goiter	**N (%)**	**74 (72.55%)**
Recurrent Goiter	**N (%)**	**9 (8.8%)**
Surgical procedure		
Total Thyroidectomy	**N (%)**	**104 (84.55%)**
Total thyroidectomy with block neck dissection N(%)		**19 (15.45%)**

31 (25.2%) of the included patients suffered of post-operative hypocalcemia with a mean Calcium drop from preoperative to postoperative of 1.46 ± 0.42) (Table 2).

Table (2): Intra-operative identification of parathyroid glands and postoperative calcium drop

Variable		No of patients =123 (100%)
Number of para thyroid glands identified in the operation		
0	**N (%)**	**4 (3.25%)**
1	**N (%)**	**5 (4.07%)**
2	**N (%)**	**14 (11.38%)**
3	**N (%)**	**12 (9.75%)**
4	**N (%)**	**88 (71.55%)**
Calcium drop from preoperative to postoperative (24 h) Mean ± SD		**1.46 ± 0.42)**
Postoperative early hypocalcemia (ca < 8.0 mg /dl)		
Yes	**N (%)**	**31 (25.2%)**
No	**N (%)**	**92 (74.8%)**

Table (3) showed that there was a statistically significant correlation between female sex and hypocalcemia (P < 0.0001*). Hypocalcemia was statistically significant evident in the age group between 40-50 years.

Table (3): Correlation between sociodemographic data and hypocalcemia

Variable		Hypocalcemia 31(25.2%)	Normocalcemia 92(74.8%)	P value
Sex				
Female	**N (%)**	**28 (90.3%)**	**71 (77.2%)**	**< 0.0001***
Male	**N (%)**	**3 (9.7%)**	**21 (22.8%)**	**0.073**
Age	**Mean ± SD**	**44.56 ± 11.24**	**47.58 ± 11.98**	**0.22**
Age groups				
< 40	**N (%)**	**6 (19.35%)**	**39 (42.4%)**	**0.062**
40-50	**N (%)**	**14 (45.16%)**	**21 (22.8%)**	**< 0.0001***
50-60	**N (%)**	**8 (25.8%)**	**21 (22.8%)**	**0.32**
> 60	**N (%)**	**3 (9.7%)**	**11 (11.95%)**	**0.89**
Co morbidities				
DM	**N (%)**	**3 (9.7%)**	**14 (15.2%)**	**0.065**
Hypertension	**N (%)**	**3 (9.7%)**	**11 (11.95%)**	**0.43**
IHD	**N (%)**	**1 (3.24%)**	**3 (3.26%)**	**0.76**

Table (4) demonstrated that malignant goiter, Grave's disease and recurrent goiter were significantly correlated with the incidence of postoperative hypocalcemia. Also total thyroidectomy with block neck dissection was strongly correlated with the incidence of postoperative hypocalcemia (p< 0.0001*). There was a statistically significant calcium drop from pre-operative to post-operative levels in hypocalcemic group more than in normocalcemic group.

Table (4): Correlation between histopathological findings and surgical procedure with incidence of hypocalcemia

Variable		Hypocalcemia 31	Normocalcemia 92	P value
Definitive histological diagnosis				
Malignant	**N (%)**	**17 (54.84%)**	**4 (4.35%)**	**< 0.0001***
Benign	**N (%)**	**14 (45.16%)**	**88 (95.65%)**	**0.09**
Graves' Disease	**N (%)**	**5 (16.13%)**	**8 (8.7%)**	**0.021***
Thyroiditis	**N (%)**	**2 (6.45%)**	**2 (2.18%)**	**0.048***
Nodular Goiter	**N (%)**	**2 (6.45%)**	**74 (84.1%)**	**0.012***
Recurrent Goiter	**N (%)**	**5 (16.13%)**	**4 (4.35%)**	**< 0.0001***
Surgical procedure				
Total Thyroidectomy N (%)		**14 (45.16%)**	**90 (97.82%)**	**0.042***
Total thyroidectomy with block neck dissection N (%)		**17 (54.84%)**	**2 (2.18%)**	**< 0.0001***
Number of para thyroid glands identified in the operation				
0		**2 (6.45%)**	**3 (3.26%)**	**0.34**
1		**4 (12.9%)**	**4 (4.35%)**	**0.39**
2		**2 (6.45%)**	**10 (9.2%)**	**0.22**
3		**6 (19.35%)**	**6 (6.52%)**	**0.63**
4		**17 (54.84%)**	**71 (77.18%)**	**0.08**
Calcium drop from preoperative to postoperative (24 h) Mean ± SD		**1.78 ± 0.87**	**0.95 ± 0.12**	**< 0.0001***

DISCUSSION

Hemorrhage, recurrent laryngeal nerve palsy, and hypocalcemia following thyroidectomy are just a few of the surgical problems that might result from a total thyroidectomy. The most serious of these complications is hypocalcemia, which needs to be treated right away due to the possibility of tetany, bronchospasm, and cardiac arrhythmias [3, 7]. The occurrence of hypocalcemia and its predictive indicators after complete thyroidectomy were the main subjects of the current investigation.

Managing patients with persistent hypocalcemia might provide challenges. They can also suffer from severe morbidity, although many are kept well with a consistent calcium and vitamin D routine, which calls for sporadic laboratory testing. Utilizing techniques to avoid hypocalcemia and lessen its symptoms is crucial for thyroid surgeons [15]. Some authors [16] reported hypocalcemia with old age, while others [17, 18] reported it in younger age.

In the current study the most common incidence of hypocalcemia occurred at the age group from 40-50 years (45%) followed by 25% occurred in age group 50-60 years. This can be explained by the concomitant cancer thyroid in these groups of age in the current study.

Ebril *et al.* [19] and others [5, 21, 22] reported more post thyroidectomy hypocalcemia in women. This matches the result of the current study. This is assumed to be due to more incidence of thyroid diseases in females with subsequent liability to more complications. Also, hormonal changes and variations can be a cause. This also matches **Sands *et al.*** [9] and **Del Rio** [8] who reported a higher incidence in women and this emphasized the effects of hormonal variations on calcium homeostasis.

Patients with Graves' disease (GD) are significantly more likely to suffer parathyroid and recurrent laryngeal nerve damage, according to numerous studies. When GD was compared to those without this illness, the rates of both temporary and persistent hypocalcemia were significantly greater [7]. As a result, before surgery, GD patients need to be properly monitored. These findings were in line with the current results where a statistically significant incidence of hypocalcemia was found in patients suffering from Greve's disease and this is assumed to the high vascularity that is evident in GD especially when not controlled making dissection to some extent difficult with liability for parathyroid injury or compromise of the blood supply to the parathyroid glands.

Hypocalcemia was more common in patients with Hashimoto thyroiditis (HT) [23, 24]. The reason could be that individuals with HT may have more vulnerable parathyroid glands, either because of inflammation and difficult mobilization of the gland requiring extra retraction. Furthermore, HT increases fibrosis, which makes it more difficult to identify the parathyroid gland accurately, especially when a junior surgeon is performing the surgery. These findings match the current results which showed that patients with HT experienced statistically significant hypocalcemia.

Patients with thyroid cancer who underwent CLND may experience hypocalcemia as a result of vascular injury or an unintentional parathyroidectomy brought on by thyroid capsule invasion. Compared to the upper parathyroid glands, which are typically spared injury, the lower glands are more vulnerable. In CLND, damage to the lower parathyroid gland is frequently inevitable [7]. Hypocalcemia is therefore more common in thyroid cancer patients undergoing CLND. The results of the current investigation, showed a considerable incidence of both temporary and permanent hypocalcemia following surgery in patients with malignant nodules, which are consistent with several studies [2, 17, 25] that have revealed that thyroid malignancy enhanced the development of hypocalcemia. Following surgery, patients with TT may experience hypocalcemia due to avascular necrosis of the parathyroid glands caused by the excision of lymph and adipose tissue [26]. According to studies, there is a 27.5% chance of experiencing temporary hypocalcemia following TT [27].

The current study's findings showed that one of the primary risk factors for postoperative hypocalcemia is TT. Extensive thyroidectomy and lymphatic dissection could substantially raise the risk of parathyroid gland injury during surgery. Therefore, in order to prevent needlessly broadening the scope of surgery, suitable surgical techniques should be chosen in accordance with the patient's disease type.

Study Limitations

This research had certain restrictions. Firstly, a larger degree of heterogeneity in the research for variations in surgical techniques and postoperative care resulted from the identical investigations being carried out globally. Second, the results of the included studies may have been impacted by the fact that surgeons with a low amount of thyroid surgery experience are more likely to experience difficulties following TT. Third, the analysis of some of the risk factors only comprised a limited number of research. The results of this study have some discrepancies that suggest areas for further investigation. Large sample size multicenter trials should be carried out to determine the risk factors for postoperative hypocalcemia.

CONCLUSION

According to the current results, malignant goiter, Grave's disease and recurrent goiter were independent risk factors for post total thyroidectomy hypocalcemia.

Financial support and sponsorship: Nil.
Conflicts of interest: Nil.

REFERENCES

1. **Harris A, Prades E, Tkachuk O, Zeitoun H (2016):** Better consenting for thyroidectomy: who has an increased risk of postoperative hypocalcemia? Eur Arch Otorhinolaryngol., 273 (12): 4437–43.
2. **Sitges A, Ruiz S, Girvent M, Manjon H *et al.* (2010):** Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg., 97 (11): 1687–95.
3. **Joseph R, Edirimanne S, Eslick D (2018):** Thyroidectomy for thyroid cancer in the elderly: A meta-analysis. Eur J Surg Oncol.,45 (3): 310–7.
4. **Imran S, Chu K, Rajaraman M, Rajaraman D *et al.* (2019):** Primary versus Tertiary Care Follow-Up of Low-Risk Differentiated Thyroid Cancer: Real-World Comparison of Outcomes and Costs for Patients and Health Care Systems. Eur Thyroid J., 8 (4): 208–14.
5. **Lang B, Chan T, Chow C (2016):** Visualizing fewer parathyroid glands may be associated with lower hypoparathyroidism following total thyroidectomy. Langenbecks Arch Surg., 401 (2): 231–8.
6. **Falch C, Hornig J, Senne M, Braun M *et al.* (2018):** Factors predicting hypocalcemia after total thyroidectomy - A retrospective cohort analysis. Int J Surg., 55: 46–50.
7. **Qin Y, Sun W, Wang Z, Dong W *et al.* (2021):** A Meta-Analysis of Risk Factors for Transient and Permanent Hypocalcemia after Total Thyroidectomy. Front Oncol., 24 (10): 614-9.
8. **Del Rio P, Rossini M, Montana C, Viani L *et al.* (2019):** Postoperative hypocalcemia: analysis of factors influencing early hypocalcemia development following thyroid surgery. BMC Surg.,18 (1): 25-31
9. **Sands N, Payne R, Côté V, Hier M *et al.* (2011):** Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. Otolaryngol Head Neck Surg.,145 (4): 561–4.
10. **Ozemir I, Buldanli M, Yener O, Leblebici M *et al.* (2011):** Factors affecting postoperative hypocalcemia after thyroid surgery: importance of incidental parathyroidectomy. North Clin Istambul, 3 (1): 9–14.
11. **Del Rio P, Iapichino G, De Simone B, Bezer L *et al.* (2010):** Is it possible to identify a risk factor condition of hypocalcemia in patients candidates to thyroidectomy for benign disease? Annal Ital Chir., 81 (6): 397–401.
12. **Kakava K, Tournis S, Papadakis G, Karelas I *et al.* (2010):** Postsurgical hypoparathyroidism: a systematic review. In vivo, 30 (3): 171–80.
13. **Cranshaw I, Moss D, Whineray E, Harman C *et al.* (2007):** Intraoperative parathormone measurement from the internala jugular vein predicts postthyroidectomy hypocalcemia. Langenbeck's Arch Surg., 392 (6): 699–702.
14. **Calò P, Conzo G, Raffaelli M, Medas F *et al.* (2017):** Total thyroidectomy alone versus ipsilateral versus bilateral prophylactic central neck dissection in clinically node-negative differentiated thyroid carcinoma.A retrospective multicenter study. Eur J Surg Oncol., 43 (1): 126–32.
15. **Stack B, Bimston D, Bodenner D, Brett E *et al.* (2015):** American Association Of Clinical Endocrinologists And American College Of Endocrinology Disease State Clinical Review: Postoperative Hypoparathyroidism–Definitions And Management. Endocr Pract., 21 (10): 674–85.
16. **Eismontas V, Slepavicius A, Janusonis V, Zeromskas P *et al.* (2018):** Predictors of postoperative hypocalcemia occurring after a total thyroidectomy: results of prospective multicenter study. BMC Surg., 18 (1): 55–5.
17. **Kala F, Sarici I, Ulutas K, Sevim Y *et al.* (2015):** Intact parathormone measurement 1 hour after total thyroidectomy as a predictor of symptomatic hypocalcemia. Int J Clin Exp Med., 8 (10): 18813–8.
18. **Mahmoud R, Neto V, Alves W, Lin C *et al.* (2016):** Hypomagnesemia associated with hypocalcemia after total thyroidectomy: an observational study. Magnes Res., 29 (2): 43–7.
19. **Erbil Y, Barbaros U, Temel B, Turkoglu U *et al.* (2009):** The impact of age, vitamin D(3) level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. Am J Surg., 197 (4): 439–46.
20. **Docimo G, Ruggiero R, Casalino G, Docimo L *et al.* (2017):** Risk factors for postoperative hypocalcemia. Updates Surg., 69 (2): 255–60.
21. **Luo H, Zhao W, Yang H, Su A *et al.* (2018):** In Situ Preservation Fraction of Parathyroid Gland in Thyroidectomy: A Cohort Retrospective Study. Int J Endocrinol.,74 (9): 31-43
22. **Nair C, Babu M, Menon R, Jacob P (2013):** Hypocalcaemia following total thyroidectomy: An analysis of 806 patients. Indian J Endocrinol Metab., 17 (2): 298–303.
23. **Shih M, Lee J, Hsieh C, Yu J *et al.* (2008):** Thyroidectomy for Hashimoto's thyroiditis: complications and associated cancers. Thyroid, 18 (7): 729–34.
24. **Roh J, Park C (2006):** Intraoperative parathyroid hormone assay for management of patients undergoing total thyroidectomy. Head Neck, 28 (11): 990–7.
25. **Tian W, Jiang Y, Gao B, Zhang B *et al.* (20014):** Application of nano-carbon in lymph node dissection for thyroid cancer and protection of parathyroid glands. Med Sci Monit.,14 (20): 1925–1930.
26. **Nam K, Yun J, Lee Y (2008):** Hypocalcemia after Total Thyroidectomy: Incidence and Risk Factors. J Korean Surg Soc.,74 (2): 182–186.
27. **Rodelo-Haad C, Pendon-Ruiz M, Dıaz-Tocados J *et al.* (2020):** The Role of Disturbed Mg Homeostasis in Chronic Kidney Disease Comorbidities. Front Cell Dev Biol., 12 (8): 543-49.