The prevalence of hypocalcemia following total thyroidectomy. *A retrospective study based at King Abdulaziz University Hospital, Jeddah, Saudi Arabia*

Fatma K. Althoubaity, *MBBS, FRCSI,*
Sultan A. Almusallam, *Medical Student,*
Abdullah S. Alghorair, *Medical Student,*
Faisal S. AlQahtani, *Medical Student,*
Omar M. Khotani, *Medical Student,*
Naif F. Bamakhish, *Medical Student,*
Ammar D. Alzriri, *Medical Student.*

ABSTRACT

Objectives: To estimate the prevalence of hypocalcemia following total thyroidectomy (TT) at a tertiary center.

Methods: This retrospective study was conducted between 2014 and 2019 at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. The study was based at the Department of General Surgery and was approved by the Research Ethics Committee of KAUH. Medical records of 154 patients who had undergone TT were reviewed. Data such as age, gender, level of postoperative calcium at 24 and 48 hours after surgery, parathyroid hormone (PTH) levels, central neck dissection (CCND), histological diagnosis were entered into Microsoft Excel sheets.

Results: Hypocalcemia occurred more on the second day after surgery in 67.4% of patients. Among them, 83.9% were female and 16.1% were male. The majority of patients were asymptomatic and benign thyroid disease was the most common. There was a significant association between hypocalcemia and the PTH level (p<0.001).

Conclusion: There was a high prevalence of hypocalcemia on the second day after surgery. Presence of hypocalcemia association with the PTH level. Meticulous surgical technique and preservation of parathyroid vascularity are important in preventing postoperative hypocalcemia.

Keywords: hypocalcemia, thyroid diseases, total thyroidectomy

Saudi Med J 2020; Vol. 41 (4): 431-434
doi: 10.15537/smj.2020.4.25045

Hypocalcemia is a common complication of total thyroidectomy (TT) and can be either transient or permanent.[1] The prevalence of permanent hypocalcemia was 0.11%, while the prevalence of transient hypocalcemia 7%.[2] There are many causes of postoperative hypocalcemia (PoSH), including accidental damage or devascularization of the blood supply to the parathyroid gland during the procedure. In addition, "hungry bone" syndrome, which is an increase in the blood calcium absorption rate by the bones, may occur.[3,4] Hypocalcemia manifests as perioral and aural parasthesia, vocal cord paralysis, abnormal dermal sensations, involuntary muscle contractions, convulsions, and a prolonged electrocardiogram QT interval. Congestive heart failure may also occur.[5] The risk of hospitalization markedly increases in the period immediately following TT due to the symptoms of hypocalcemia.[2]

Previous studies have proposed risk factors for hypocalcemia. Among them, female gender, older age, hyperthyroidism, thyroid malignancy, undergoing a follow-up surgical procedure, sub-sternal localization of thyroid tissue, undergoing cervical lymph node dissection, and having an enlarged thyroid gland have been suggested as factors associated with increase in risk of hypocalcemia.[6] Finally, the risk of PoSH has been reported to increase with age, which is associated with vitamin D deficiency.[7] A previous study that examined the predictors of PoSH in patients undergoing TT has reported that 64.2% of patients had become hypocalcemic.[1] Nevertheless, the evidence regarding the prevalence of PoSH is insufficient in Saudi Arabia. The present study aim to estimate the prevalence of hypocalcemia among patients who had undergone TT at King Abdul-Aziz University Hospital (KAUH), Jeddah, Saudi Arabia.

Methods. This retrospective study was conducted between 2014 and 2019 at KAUH, a tertiary center in Jeddah, Saudi Arabia. The study was based at the Department of General Surgery and was approved by the Research Ethics Committee of KAUH. Medical records of 154 patients who had undergone TT were reviewed.

Information extracted from the medical records and entered by Microsoft Excel sheet 2010 included data on age, gender, histological diagnosis, level of postoperative calcium at 24 and 48 hours after surgery, parathyroid hormone (PTH) levels, details of central neck dissection (CCND), symptoms of hypocalcemia, and vitamin D and calcium supplements. Patient with calcium level <2.12 mmol/L (normal level 2.12mmol/L

to 2.52 mmol/L). Patient with PTH <1.18 mmol/L (normal level 1.18 mmol/L to 8.43 mmol/L).

All surgeries were carried out by experts who were well-trained in TT procedure. All patients were informed regarding the risk of this procedure and provided consent. Patients were eligible for inclusion if they were aged 18 years or above and had undergone TT. There were no exclusion criteria. The occurrence of hypocalcemia was the primary outcome.

Statistics analysis. Information were extracted from the medical records and entered using a Microsoft 2010 Excel sheet. Statistical Package for Social Sciences version 21 (IBM Corp, Armonk, NY, USA) was used for analyses. Continuous variables are reported as means and standard deviations. Additionally, categorical variables are reported as frequencies and percentages. Further, we used Chi-square test to evaluate the relationship between the qualitative variables. A *p*-value <0.05 was considered statistically significant.

Results. Among 154 patients who had undergone TT, there were 127 (82.5) females and 27 (17.5%) males. The mean age of patients at the time of surgery was 43.23±12.16 years (Table 1). Calcium levels measured on 2 consecutive days post-surgery demonstrated that the frequency of hypocalcemia was the highest on the second day, when it was detected in 87 (67.4%) patients, with a mean calcium level of 2.03±0.17 mmol/L (normal range, 2.12 mmol/L–2.52 mmol/L) (Table 2). Among patients with hypocalcemia, there were 73 (83.9%) females and 14 (16.1%) males. The majority of patients had asymptomatic hypocalcemia; symptomatic patients (n=18, 20.7%) complained of numbness. In addition, 50 (57.5%) hypocalcemia patients had benign disease, and 37 (42.5%) had malignant disease. Among the patients with hypocalcemia, 31 (91.2%) developed hypoparathyroidism, while 6 (8.8%) developed hyperparathyroidism. There was a significant relationship between hypocalcemia and PTH level. However, there was no relationship between hypocalcemia and gender, type of disease, and CCND status or postoperative supplement prescribed (Table 3).

Discussion. Over the past several years, TT has become popular as treatment for benign and malignant thyroid disease due to its effectiveness in preventing disease recurrence and lowering the risk of corrective surgeries.[8] However, the risk of hypocalcemia increases after TT, leading to patient distress, prolonged hospitalization, increased use of healthcare resources, and higher treatment costs.[9] This study aimed to report the prevalence of hypocalcemia among patients who had undergone TT at the KAUH.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Table 1 - Demographic and clinical characteristics of patients who had undergone total thyroidectomy (N=154).

Factors	n (%)
Gender	
Male	27 (17.5)
Female	127 (82.5)
Histopathology diagnosis	
Benign	77 (50.0)
Malignant	77 (50.0)
Neck dissection	
Performed	40 (26.0)
Not performed	114 (74.0)
Age (mean±SD)	43.23±12.16

SD: standard deviation

Table 2 - The prevalence of hypocalcemia at 24 and 48 hours after total thyroidectomy, including mean calcium levels at corresponding ti me points.

Interval	n (%)
At 24 hours postoperatively	91 (65)
At 48 hours postoperatively	87 (67.4)
	Mean±standard deviation
At 24 hours postoperatively	2.06±0.14 mmol/L
At 48 hours postoperatively	2.03±0.17 mmol/L

Table 3 - Correlation between various variables and calcium level at 48 hours after total thyroidectomy.

Variables	Yes	No	*P*-value[α]
Gender			
Male	14 (58.3)	10 (41.7)	0.416
Female	73 (69.5)	32 (30.5)	
Histology			
Benign	50 (75.8)	16 (38.1)	0.061
Malignant	37 (58.7)	26 (41.3)	
Neck dissection			
Yes	24 (66.7)	12 (33.3)	1.00
No	63 (67.7)	30 (32.3)	
Parathyroid hormone level			
Normal	31 (50.0)	31 (50.0)	
Hypoparathyroidism	31 (91.2)	3 (8.8)	<0.001
Hyperparathyroidism	6 (100)	0	
Medication supplements			
Yes	79 (67.5)	38 (32.5)	1.00
No	8 (66.7)	4 (33.3)	

Values are presented as numbers and percentages (%). [α]Chi-square test

In this study, women were more likely to develop hypocalcemia after TT than men. In addition, previous studies have reported similar findings; however, they were statically non-significant.[10] The present finding is in line with the previous studies that have reported a statistically significant association.[11] Taylor et al[12] have reported that women are generally more likely to develop thyroid diseases than men, which, in turn, increases their risk of requiring and undergoing surgery. However, it should be noted that the literature was inconsistent regarding the relationship between gender and hypocalcemia. In this study, the sample distribution was skewed toward females, which might have affected the relationship between hypocalcemia and gender.

In our study, there was a high prevalence of hypocalcemia after thyroidectomy, in particular, on the second day after surgery, when it was detected in 67.4% of patients. This finding is in line with previous studies, where hypocalcemia was reported as most likely to occur 48 hours after surgery, with an estimated 3.4% of patients affected.[12] A separate study, conducted between 2012 and 2016, has shown that hypocalcemia occurred in 21.4% of patients 24 hours after surgery.[13] These discrepancies might have resulted from the differences in age between the samples under study (the mean age in our study was 43.23 years); thus, older adults might be more prone to hypocalcemia due to decrease in the availability of calcium ions.[13]

Concurrently, patients in the present study who developed hypocalcemia were more likely to have benign thyroid disease; although, this finding is not statistically significant. This is in contrast to previous studies, which have shown that patients with malignant conditions are more likely to develop hypocalcemia.[2,14]

Nevertheless, a literature review has indicated that the prevalence of hypocalcemia was higher among patients with benign thyroid disease, which might be due to the increase in size and vascularity of the thyroid gland associated with benign diseases, such as graves and multinodular goiter, which may cause difficulties during operation.[13] However, other studies have illustrated that malignant conditions were more likely to be associated with a comorbid hypocalcemia.[2,14] The plausible underlying mechanism might be related to the attachment and fusion of the thyroid capsule and the parathyroid glands, which might be damaged during CCND.[15]

Additionally, a retrospective study showed that CCND might increase the risk of hypocalcemia following TT, and there is a significant association between CCND and hypocalcemia (p=0.049).[10] In the present study, a similar association was not detected, most likely due to a relatively small proportion of patients who had undergone CCND, which was 26%. However, the previous finding might be linked to the parathyroid gland injury sustained during surgery due to increased volume or an error during a lymph node dissection, which might result in hypoparathyroidism and hypocalcemia.[13] This study aimed to improve cost-effectiveness by decreasing PoSH and to improve patient health after the operation. However, there are not enough studies on this topic in Saudi Arabia; hence, more studies are required to support these findings.

Study limitations. First, this was a retrospective study. A large number of patients included in the present study had missing data on the size and weight of the thyroid gland, and there was no long-term follow-up of patients after discharge to collect data on medications used. Second, there was variability in the time of calcium level measurement, with a few measurements occurring later than the second day after surgery. In addition, documentation regarding patient status and progress was poor.

In conclusion, this study aimed to report the prevalence of hypocalcemia among patients who had undergone TT at the KAUH. We found a high prevalence of hypocalcemia after thyroidectomy, especially on the second day following surgery. In addition, our findings showed a significant relationship between hypocalcemia on the second day after surgery and the PTH level (p<0.05). Meticulous surgical technique and preservation of parathyroid vascularity are crucial in preventing PoSH.

The present findings can be used to improve the cost-effectiveness of resource allocation appropriate for hypocalcemia to enhance the quality of life of patients undergoing TT. As existing evidence regarding the prevalence of PoSH remains insufficient, further studies on the prevalence of PoSH are required, particularly on surgical technique or other variables that affect the risk of hypocalcemia.

Acknowledgment. *We would like to thank the students enrolled in the Research Summer School 2019 for helping us with this paper. We would like to thank Editage (https://www.editage.com) for English language editing.*

Received 6th October 2019. Accepted 11th March 2020.

From the Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

Addressed correspondence to: Dr. Sultan A. Almusallam, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia. E-mail: sultanalmusallam1418@gmail.com
ORCID ID: https://orcid.org/0000-0003-3176-8226

References

1. Eismontas V, Slepavicius A, Janusonis V, Zeromskas P, Beisa V, Strupas K, et al. Predictors of postoperative hypocalcaemic occurring after a total thyroidectomy: results of prospective multicenter study. *BMC Surg* 2018; 18: 55.
2. Baloch N, Taj S, Anwer M, Naseem M. Frequency of hypocalcaemia following total thyroidectomy. *Pak J Med Sci* 2019; 35: 262-265.
3. Algarni M, Alzahrani R, Dionigi G, Hadi AH, AlSubayea H. Parathyroid hormone and serum calcium levels measurements as predictors of postoperative hypocalcaemic in totalthyroidectomy. *Gland Surg* 2017; 6: 428-432.
4. Jain N, Reilly RF. Hungry bone syndrome. *Curr Opin Nephrol Hypertens* 2017; 26: 250-255.
5. Aqtashi B, Ahmad N, Frotzler A, Bähler S, Linder T, Müller W. Risk factors for hypocalcaemia after completion hemithyroidectomy in thyroid cancer. *Swiss Med Wkly* 2017; 147: e14513.
6. Lale A, Öz AB, Akcan AC, Sözüer EM, Arıkan TB, Gök M. Determination of risk factors causing hypocalcaemia after thyroid surgery. *Asian J Surg* 2019; 42: 883-889.
7. Edafe O, Balasubramanian SP. Incidence, prevalence and risk factors for post-surgical hypocalcaemia and hypoparathyroidism. *Gland Surg* 2017; 6: S59-S68.
8. Hu J, Zhao N, Kong R, Wang D, Sun B, Wu L. Total thyroidectomy as primary surgical management for thyroid disease: surgical therapy experience from 5559 thyroidectomies in a less-developed region. *World J Surg Oncol* 2015; 14: 20.
9. De Pasquale L, Sartori PV, Vicentini L, Beretta E, Boniardi M, Leopaldi E, et al. Necessity of therapy for post-thyroidectomy hypocalcaemia: a multi-centre experience. *Langenbecks Arch Surg* 2015; 400: 319-324.
10. Arman S, Vijendren A, Mochloulis G. The incidence of post-thyroidectomy hypocalcaemia: a retrospective single-centre audit. *Ann R Coll Surg Engl* 2019; 14: 1-6.
11. Kakava K, Tournis S, Papadakis G, Karelas I, Stampouloglou P, Kassi E, et al. Postsurgical hypoparathyroidism: a systematic review. *In vivo* 2016; 30: 171-179.
12. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. *Nat Rev Endocrinol* 2018; 14: 301-316.
13. Chereau N, Vuillermet C, Tilly C, Buffet C, Trésallet C, du Montcel ST, et al. Hypocalcaemic after thyroidectomy in patients with a history of bariatric surgery. *Surg Obes Relat Dis* 2017; 13: 484-490.
14. Del Rio P, Rossini M, Montana CM, Viani L, Pedrazzi G, Loderer T, et al. Postoperative hypocalcaemic : analysis of factors influencing early hypocalcaemic development following thyroid surgery. *BMC Surg* 2019; 18: 25.
15. Zheng J, Song H, Cai S, Wang Y, Han X, Wu H, et al. Evaluation of clinical significance and risk factors of incidental parathyroidectomy due to thyroidectomy: A single-center retrospective clinical study. *Medicine (Baltimore)* 2017; 96: e8175.