Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Original Research Article

Hypocalcemia in Total Thyroidectomy with Central Block Dissection for Pap Ca Thyroid with Nodal Metastasis

Dr. Abdul Latheef A.[1], Dr. Nijas N.A.[2], Dr. Fouzia B.[3]

[1]Retired Professor & HOD, Department of General Surgery, Government Medical College, Trivandrum, Kerala, India, Senior Consultant Surgeon, TSC Hospital, Trivandrum, Kerala, India.
[2]Consultant Surgeon, TSC Hospital, Trivandrum, Kerala, India.
[2]Associate Professor, Department of Obstetrics & Gynaecology, Government Medical College, Malappuram, Kerala, India.

Corresponding Author
Dr. Nijas N.A., Consultant Surgeon, TSC Hospital, Trivandrum, Kerala, India.

Received: 11-09-2024 / Revised: 27-09-2024 / Accepted: 13-11-2024

ABSTRACT

Background
Hypocalcemia is a serious problem following thyroid surgery. Preventing this condition is essential to evade lifelong supplementation of vitamin D & calcium . The aim of present study was to evaluate the rate of hypocalcemia in total thyroidectomy with central block dissection for Papillary carcinoma of thyroid with nodal metastasis.

Methods
The present prospective study was conducted among 160 patients of papillary carcinoma with nodal metastasis at department of surgery of a tertiary care center during the time period of three years. Patients diagnosed with PtC with nodal metastasis underwent total thyroidectomy & CND, followed by a six-month evaluation of hypocalcaemia. Results were analyzed suing SPSS version 25.0.

Results
Out of 160 patients only 40 patients (25%) showed hypocalcemia after total thyroidectomy. Patients were divided into 3 groups: group A normocalcemic- 120 (75%), group B hypocalcemic euparathyroid- 30 (18.75%) & hypoparathyroid- 10 (6.25%). Comparison of clinicopathological parameters showed significant results among the three groups for tumor size, invasion, calcium level & TNM staging.

Conclusion
The surgical approach is the primary risk factor for post-thyroidectomy hypocalcemia. Proper dissection & handling of parathyroid tissue are crucial for conserving the glands & their blood supply. Additional risk factors include big tumors, & late stages.

Keywords: central neck dissection, Hypocalcemia, parathyroid, thyroidectomy, papillary carcinoma.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

INTRODUCTION

Papillary thyroid carcinoma (PtC) is a subtype of well-differentiated thyroid carcinoma (wdtC), alongside follicular & Hürthle cell carcinoma. Nonetheless, PtC is significantly more prevalent than the other two variants of wdtC, constituting 70% to 90% of all instances of thyroid malignant neoplasms. [1-4] The prevalence of PtC was escalating swiftly until the onset of the previous decade, with a female to male ratio of 3:15.[5] The positive aspect of this elevated occurrence is that papillary thyroid carcinoma (PtC) is regarded as the least malignant kind of thyroid carcinomas.

The contemporary care of papillary thyroid carcinoma (PtC) involves primary surgical intervention, postoperative radioiodine therapy, & TSH-suppressive hormonal therapy, guided by initial risk classification & therapeutic response throughout follow-up.[6] It is recommended that all high-risk patients undergo complete thyroidectomy. [7,8] The criteria for performing a complete thyroidectomy following a diagnosis of papillary thyroid carcinoma should align with those for total thyroidectomy. Completion thyroidectomy may be executed within 7 days (very early completion thyroidectomy), between 8 days & 3 months (early completion thyroidectomy), or beyond 3 months post-primary surgery (delayed completion thyroidectomy).[9]

The parathyroid glands, situated near the thyroid gland, play a crucial role in maintaining calcium homeostasis in the blood by secreting parathyroid hormone (PTH).[10] Postoperative hypocalcaemia may emerge as a potential complication after surgical treatments, presenting as either a transient or persistent illness. [11] The initial signs of hypocalcemia primarily include neuromuscular symptoms &, on occasion, psychotic episodes. Ectodermal alterations resulting in baldness, dermatitis, & cataracts may manifest as early as six months post-operation.

Chronic hypocalcaemia can lead to brain lesions & heart arrhythmias. Chronic hypocalcaemia significantly affects patient health & incurs huge financial losses. [12]

AIM

The aim of present study was to evaluate the rate of hypocalcemia in total thyroidectomy with central block dissection for Papillary carcinoma of thyroid with nodal metastasis.

MATERIAL & METHODS

The present prospective study was conducted at department of surgery of a tertiary care center during the time period of three years. Ethical clearance was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure.

Through convenience sampling a total of 160 patients of papillary carcinoma of thyroid with nodal metastasis were selected on the basis of inclusion & exclusion criteria.

Inclusion criteria

Patients diagnosed with papillary thyroid carcinoma with nodal metastasis underwent total thyroidectomy & central neck dissection, followed by a six-month evaluation of hypocalcaemia through the measurement of postoperative total & ionized calcium levels in all patients, as well as PTH levels in those exhibiting hypocalcaemia. The diagnosis of patients was determined using a comprehensive history, neck ultrasonography, neck CT for advanced cases, meticulous clinical examination, & pathological assessment via FNAC.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Exclusion criteria

The exclusion criteria encompassed hypoparathyroidism, a prior history of neck surgery, patients undergoing iodine therapy, & individuals with calcium metabolism abnormalities.

A comprehensive history was examined for all patients, & data was gathered concerning age, history, gender & medication history. A comprehensive physical examination was conducted, encompassing indirect laryngoscopy & voice assessment. Preoperative laboratory studies included free T3, free T4, TSH, serum total calcium, & ionized calcium. Neck ultrasonography was performed on all patients, whereas CT scans were reserved for those with advanced malignancies. Fine needle aspiration cytology (FNAC) was performed on all patients for pathological analysis, & only cases of WDC were included. Participants in this research underwent extracapsular total thyroidectomy accompanied by bilateral central node dissection, with meticulous care taken to preserve all parathyroid glands & their vascular supply by transecting the branches of the inferior thyroid arteries that supply the thyroid gland while conserving the primary ITA & their branches to the parathyroid glands. Total & ionized calcium levels were assessed on the first day following surgery. In hypocalcemic instances, parathyroid hormone (PTH) levels were assessed, & serum calcium levels were monitored more closely.

All hypocalcaemic patients commenced calcium & vitamin D supplementation, accompanied by attempts to taper off, while concurrently monitoring serum calcium levels.

Follow-up appointments were arranged for all subjects after 1, 2 & 6 months. During each appointment, a thyroid hormone profile & voice assessment were conducted, & blood total & ionized calcium levels were assessed. Patients were categorized into three groups: group A, normocalcaemic; group B, hypocalcaemic euparathyroid; & group C hypocalcaemia hypoparathyroid.

This study utilized POT & ionized calcium levels to detect hypocalcaemia prior to the manifestation of its signs & symptoms. PTH levels were evaluated in cases of confirmed hypocalcaemia to assess parathyroid gland function & anticipate instances of persistent hypocalcaemia. Analyzing clinicopathologic data & comparing values across various groups aids in identifying risk factors for persistent hypocalcaemia.

Statistical Analysis

Data were analysed utilizing Microsoft Excel & SPSS software for Windows (version 25.0. The constant variables were represented as mean ± SD to assess the tendency & distribution of data around the mean value.

RESULTS

In the present study 40% patients had had less than 40 years & 60% had age equal to or less than 40 years. Number of male patients were 22% while female patients were 78%. Mean mass size was 18.95 mm. 6% of patients had invasive carcinoma, 68% had focally invasive & 26% had non-invasive. According to TNM staging 78% had stage I, 12% had stage II & 10% had stage IVB. Patients were further classified according to TNM staging showed maximum patients in T1 (72%), N1b (48%) & M0 (86%) as depicted in table 1.

Characteristic		Value (%)
Age	<40	64 (40)
	≥40	96 (60)

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Sex	Male	35 (22)
	Female	125 (78)
Mass size (mm)		18.95 ±9.3
Multifocality	Single	112 (70)
	Multiple	48 (30)
Capsular invasion	Invasive	9 (6)
	Focally invasive	109 (68)
	Non invasive	42 (26)
TNM Stage	I	124 (78)
	II	20 (12)
	IVB	16 (10)
T stage	TI	115 (72)
	T2	32 (20)
	T3a	3 (2)
	T3b	6 (4)
	T4a	3 (2)
N stage	N0a	48 (30)
	N1a	35 (22)
	N1b	77 (48)
M stage	M0	138 (86)
	M1	22 (14)

Table 1 Demographic data of patients

Out of 160 patients only 40 patients (25%) showed hypocalcemia after total thyroidectomy as shown in figure 1

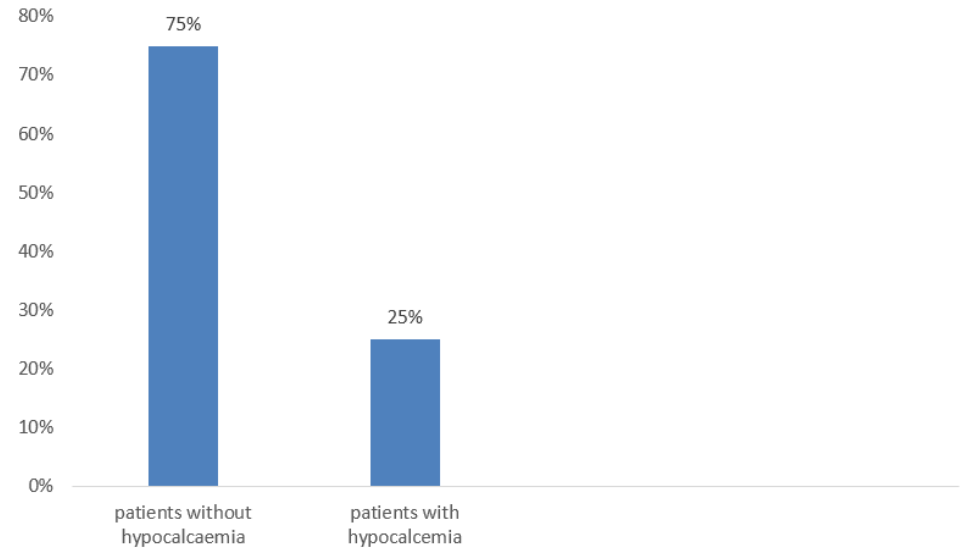

Figure 1 Prevalence of hypocalcemia

Patients were divided into 3 groups: group A normocalcemic- 120 (75%), group B hypocalcemic euparathyroid- 30 (18.75%) & hypoparathyroid- 10 (6.25%) as shown in figure 2.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

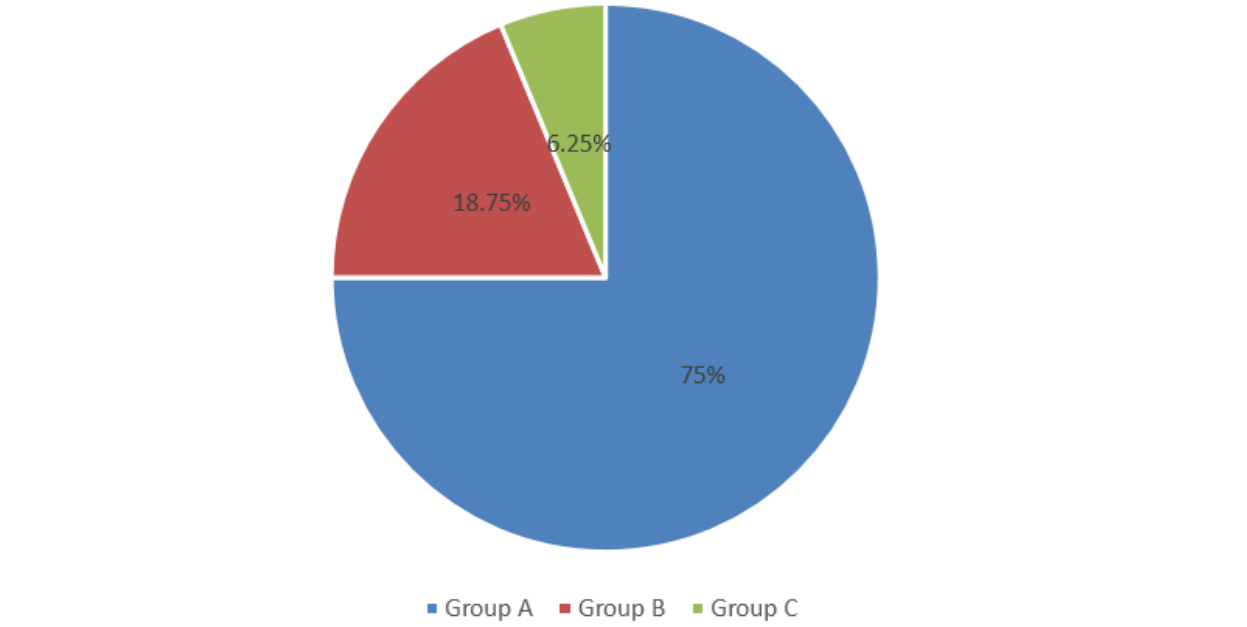

Figure 2 Division of patients according to type of condition

Compared to group C, both groups A & B reported low values for tumor size & prevalence. Patients in Group C had bigger tumors when they first arrived. While group C had cancers at later stages, including stages II & IVB, groups A & B primarily presented with early-stage malignancies. The preoperative serum ionized calcium mean was greater in Group C patients than in the other groups. Locally invasive cancers were more common in Group A than in Groups B & C. As indicated in table 2, groups B & C had lower ratios, but group A had more instances with single tumors than with multiple tumors. Significant results were observed among the three groups on comparison,

Variable		Group A	Group B	Group C	P value
Tumor size (mm)		19.56 ± 8.5	19.3 ± 10.2	24.1 ± 4.3	0.004
Multifocality	Single	90	20	2	0.003
	Multiple	30	10	8	
Extrathyroid extension	Invasive	4	4	1	0.001
	Focally invasive	90	16	3	
	No	26	10	6	
TNM stage	I	101	17	6	0.002
	II	8	9	3	
	IVB	11	4	1	
Preoperative calcium level	Total	9.62 ±0.34	8.79 ±0.14	9.07 ±0.26	0.001
	Ionized	1.07=6 ±0.10	0.91 ±0.07	1.176± 0.004	

Table 2 Comparison of clinicopathological data among three group

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

DISCUSSION

Hypocalcaemia is a significant complication that may arise after a total thyroidectomy & central neck dissection surgery. The observed phenomenon can be attributed to the physical proximity of the thyroid hormone-producing gland & the parathyroid gland, both of which play a crucial role in regulating blood calcium levels through PTH release.[13]

PTH is an 84-amino acid peptide essential for regulating calcium & phosphate levels in the blood. The chemical exhibits a relatively brief half-life of approximately 5 minutes. The regulation of secretion depends on the concentration of ionized calcium in the bloodstream, which interacts with a calcium-sensing receptor located on the cell membrane of the parathyroid glands. The activation of the G-protein coupled receptor leads to the suppression of PTH release & a decrease in blood calcium levels. An inverse sigmoidal association is evident between serum ionized calcium levels & PTH. [14]

Iatrogenic damage to the parathyroid glands is an unforeseen consequence that may arise during total thyroidectomy. The evaluation of parathyroid gland function & the identification of patients susceptible to hypocalcaemia can be efficiently accomplished through the precise measurement of serum PTH immediately post-surgery. [15]

In this study, 160 patients with thyroid papillary carcinoma with nodal metastases had their total & ionised calcium levels measured following surgery in order to assess hypocalcaemia. PTH was measured in cases with hypocalcaemia.

The prevalence of hypocalcaemia in our study was 25%, which was comparable to that of a study by Gohar MG et al. [16] They discovered that POH was present in 14 individuals (28%). They had their PTH levels checked, & four of them had hypoparathyroidism (8%), while the other ten patients had normal PTH levels (20%). PTH levels below 10 pg/ml, as assessed four hours after surgery, showed little reliability in predicting hypocalcaemia in 13.4% of participants, according to Lombardi et al. 2.1% of this group had symptoms suggestive with hypocalcaemia.[17] Postoperative PTH levels in patients with severe hypocalcaemia & related symptoms may appear normal, however this could be misleading.[18]

No clinical signs of hypocalcaemia were seen in patients in group A, & both total & ionised calcium levels were kept within the normal range. Patients in group B experienced symptoms that ranged in intensity from severe peripheral hypaesthesia to circumoral hypaesthesia & carpopedal tetany, & their total & ionised calcium levels significantly decreased below the normal range. All patients in this cohort had PTH levels that were within the normal range, with the majority falling around the lower limit (median = 23 pg/ml, sd = ±4.32). According to some authors, parathyroid insufficiency occurs when there are normal PTH levels along with clinical signs & symptoms of hypocalcaemia. [19] Group C patients exhibited overt evidence of hypocalcemia, corroborated by diminished levels of both total & ionized calcium, & indications of hypoparathyroidism reflected in their PTH levels.

Patients in Group C persisted in receiving oral calcium & vitamin D supplements for more than 6 months. [20]

Authors proposed several time intervals to delineate persistent hypocalcaemia. Certain writers proposed a six-month duration of calcium & vitamin D supplementation prior to diagnosing persistent hypocalcemia, while others recommended a one-year interval. [21]

In all patients in group B, total & ionized calcium levels normalized, leading to the cessation of oral calcium & vitamin D supplementation within an average of 16 days. This aligns with

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

established instances of post-thyroidectomy parathyroid dysfunction, when calcium levels normalize within a timeframe of one week to one month following surgery. [22]

Group C patients exhibited marginally bigger tumors & were diagnosed at more advanced stages. Preoperative calcium levels were not a risk factor, since group C patients exhibited the highest mean of ionized calcium, whereas group B patients demonstrated a lower mean of total calcium compared to group C as seen in previous study. [16]

The findings indicate that the primary mechanism responsible for postoperative hypocalcaemia is injury to the parathyroid glands due to intraoperative trauma. Depending on the severity of the trauma, parathyroid dysfunction & subsequent transient hypocalcaemia may arise from mild trauma with preserved blood supply to the glands, whereas severe trauma or unintentional ligation of their blood supply can lead to hypoparathyroidism & permanent hypocalcaemia.

CONCLUSION

The surgical technique used is the main risk factor for hypocalcaemia following thyroidectomy. The preservation of the parathyroids depends on both careful manipulation of the parathyroid tissue & thorough dissection to preserve the blood supply to the parathyroid glands. Late-stage disease, large tumour size, & advanced age are additional risk factors.

REFERENCES

1. Haymart mr, esfandiari nH, Stang mt, Sosa JA. Controver sies in the management of low-risk differentiated thyroid can cer. endocr rev. 2017;38(4):351–78.
2. Dralle H, musholt tJ, Schabram J, Steinmüller t, frilling A, Simon d, et al. German Association of endocrine Surgeons practice guideline for the surgical management of malignant thyroid tumors. langenbeck's Arch Surg. 2013;398(3):347–75.
3. Rajjoub Sr, yan H, Calcatera nA, Kuchta K, Wang C-He, lutfi W, et al. Thyroid lobectomy is not sufficient for t2 pa pillary thyroid cancers. Surgery. 2018;163(5):1134–43.
4. Blažeković i, Jukić t, Granić r, Punda m, franceschi m. An Unusual Case of Papillary Thyroid Carcinoma iodine-131 Avid metastasis to the Adrenal Gland. Acta Clin Croat. 2018; 57(2):372–6.
5. Vasileiadis i, Boutzios G, Karalaki m, misiakos e, Karatzas t. Papillary thyroid carcinoma of the isthmus: total thyroidectomy or isthmusectomy? Am J Surg. 2018;216(1):135–9.
6. Ito y, miyauchi A, Kihara m, fukushima m, Higashiyama t, miya A. overall Survival of Papillary Thyroid Carcinoma Patients: A Single-institution long-term follow-Up of 5897 Patients. World J Surg. 2018;42(3):615–22.
7. Mitchell Al, Gandhi A, Scott-Coombes d, Perros P. manage ment of thyroid cancer: United Kingdom national multidisci plinary Guidelines. J laryngol otol. 2016;130(Supl. 2):150 60.
8. Haugen Br, Alexander eK, Bible KC, doherty Gm, mandel SJ, nikiforov ye, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid nod ules & differentiated Thyroid Cancer: The American Thyroid Association Guidelines task force on Thyroid nodules & differentiated Thyroid Cancer. Thyroid. 2016;26(1):1–133.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

9. Pacini f, Schlumberger m, dralle H, elisei r, Smit JWA, Wi ersinga W, et al. european consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. eur J endocrinol. 2006;154(6):787–803.
10. Srinivasan DK, Jayabharathi K, Chandrika M, Dheen ST, Bay BH, Parameswaran R. Embryology & surgical anatomy: thyroid & parathyroid glands. In: Endocrine surgery. CRC Press; 2022:10e16.
11. Slonimsky G, Goldenberg D. Postoperative calcium man agement. In: Innovations in modern endocrine surgery. Cham: Springer; 2021:283e293.
12. Pepe J, Minisola S. A case with postsurgical hypoparathy roidism: treatment options. In: Thyroid cancer. Cham: Springer; 2021:159e166.
13. Bendary, Saied Hosny, Mohamed, Tarek Zaghlol, & Gad, Mohamed Mahmoud Mohamed. Risk Of Hypocalcemia After Total Thyroidectomy & Bilateral Central Neck Dissection In Patients With Papillary Thyroid Carcinoma. Al-Azhar International Medical Journal.2024; 5(3):20.
14. Summers R, Macnab R. The anatomical basis for preserving the blood supply to the parathyroids during thyroid surgery, & a review of current technologic advances. Anaesth Inten sive Care Med. 2017; 18:522e526.
15. Rivere AE, Brooks AJ, Hayek GA, et al. Parathyroid hormone levels predict posttotal thyroidectomy hypoparathyroidism. Am Surg. 2014; 80:817e820.
16. Gohar MG, Mohamed AE, Al-Azzouny HA. Risk of hypocalcemia after total thyroidectomy & bilateral central neck dissection in patients with well differentiated thyroid carcinoma. Al-Azhar International Medical Journal. 2020 Nov 1;1(11):139-43.
17. Lombardi CP, Raffaelli M, Princi P, et al. Parathyroid hor mone levels 4 hours after surgery do not accurately predict post-thyroidectomy hypocalcemia. 1016e1025. Surgery. 2006;140.
18. Wiseman JE, Mossanen M, Ituarte PH, et al. An algorithm informed by the parathyroid hormone level reduces hypo calcemic complications of thyroidectomy. World J Surg. 2010; 34:532e537.
19. Chhetri M, Bononi P. SUN-498 Normocalcemic Tetany: Is Parathyroid Insufficiency a Real Thing?. Journal of the Endocrine Society. 2019 Apr;3(Supplement_1):SUN-498.
20. Grigorovici A, Varcus F, Mogos S, Calin A, Hinganu D, Hinganu MV, Preda C. Hypocalcemia after Thyroidectomy for Advanced Local Malignancies. Rev Chim (Bucharest). 2019 Mar 1;70(3):1053-7.
21. Lončar I, Dulfer RR, Massolt ET, Timman R, de Rijke YB, Franssen GJ, Burger PJ, Smit C, van der Horst FA, Peeters RP, van Eijck CH. Postoperative parathyroid hormone levels as a predictor for persistent hypoparathyroidism. European Journal of Endocrinology. 2020 Aug;183(2):149-59.
22. Orloff LA, Wiseman SM, Bernet VJ, Fahey III TJ, Shaha AR, Shindo ML, Snyder SK, Stack Jr BC, Sunwoo JB, Wang MB, American Thyroid Association Surgical Affairs Committee Writing Task Force. American Thyroid Association statement on postoperative hypoparathyroidism: diagnosis, prevention, & management in adults. Thyroid. 2018 Jul 1;28(7):830-41.