

Postoperative hypo parathyroid in patient with total thyroidectomy; a multi-center study

Vinod Kumar Singhal^{1*}, Prashant Sharma², Nufra Senofer³, Adil Suleman⁴, Faris Dawood Alaswad⁵, Hatem Moussa⁶, Vidher V V Singhal⁷, Merajuddin⁸, Rafat S. Fares⁹

¹Consultant Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

²Specialist ENT Surgeon, Department of ENT Surgery, Prime Hospital, Dubai, UAE.

³Specialist ENT Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

⁴Specialist General Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

⁵Consultant General Surgeon, Department of General Surgery, Gladstone Queensland Hospital, Perth, Australia.

⁶Consultant Surgeon, Department of General Surgery, American Hospital, Dubai, UAE.

⁷Undergraduate Student UCL, London, UK.

⁸Specialist General Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

⁹Specialist General Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

***Corresponding Author:** Vinod Kumar Singha, Consultant Surgeon, Department of General Surgery, Prime Hospital, Dubai, UAE.

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Abstract:

Background: Thyroidectomy complications include nerve damage, hypoparathyroidism, and bleeding. Hypoparathyroidism, marked by reduced parathyroid function, is a common complication, leading to low calcium levels and symptoms like muscle cramps. Incidence rates vary. Surgeons must prioritize parathyroid gland identification and protection during surgery to prevent complications and ensure patient well-being.

Aim of the study: The aim of this study has been to evaluate the incidence of hypoparathyroidism and clinical manifestations of hypocalcemia after total thyroidectomy.

Methods: This retrospective study, spanning 2020-2022 across four different hospital and teaching institutes in various parts of the world, analyzed 350 patients who underwent thyroid gland surgeries, including 350 total thyroidectomies. Focused on postoperative hypoparathyroidism as an early complication. Inclusion criteria involved age (18-85), complete thyroidectomy, and no prior hypoparathyroidism. Exclusion criteria included coexisting medical conditions and pregnancy. Postoperative hypoparathyroidism diagnosis relied on low serum calcium and parathyroid hormone levels within 24 hours.

Result: The study examines the characteristics of a population undergoing thyroid surgeries. Among 144 patients, most are aged 60-65 (41.14%), with 86% females. Total thyroidectomy is standard (87.14%), while 12.86% involve lymphadenectomy. PTH levels below 15.0 pg/ml indicate potential hypoparathyroidism, more prevalent in surgeries with lymphadenectomy.

Conclusion: This multicenter study highlights a significant incidence of postoperative hypoparathyroidism after total thyroidectomy and decreased parathyroid hormone (PTH) levels. Early detection and management strategies for postoperative hypoparathyroidism are crucial, with routine monitoring of serum PTH levels within 24 hours post-surgery recommended.

keywords: postoperative, hypo parathyroid, total thyroidectomy and management protocols

Introduction

Thyroid diseases are prevalent globally, and treatment approaches vary depending on the specific disorder [1-3]. Over a decade, the incidence rate of thyroid cancer in India in women increased from 2.4 (95% CI 2.2-2.7)

to 3.9 (95% CI 3.6-4.2) [4]. Thyroidectomy, the most common surgical procedure for endocrine glands, is employed in treating various conditions such as multinodular goiter, large goiter compressing adjacent

structures, Graves' disease, nodular variant of Hashimoto thyroiditis, and amiodarone-induced thyrotoxicosis [5,6]. Total thyroidectomy and broader indications for more radical operations are emerging trends in the surgical treatment of thyroid diseases. The primary complications of thyroidectomy include permanent recurrent laryngeal nerve palsy, permanent hypoparathyroidism, transient hypocalcemia, postoperative hemorrhage, and wound infection. Hypoparathyroidism, characterized by decreased parathyroid gland function and underproduction of parathyroid hormone (PTH), is the most common complication. It can result in low blood calcium levels, leading to muscle cramping, twitching, and various symptoms. Incidence rates of temporary and permanent postoperative hypoparathyroidism vary, with rates ranging from 7-60% and 0-9%, respectively [7-9]. Postoperative hypoparathyroidism is attributed to accidental parathyroidectomy, impaired blood supply, mechanical damage, or fibrotic processes occurring in the neck post-surgery. Symptoms typically manifest 24-48 hours after surgery, with transient cases resolving within weeks to months. However, some patients experience permanent hypoparathyroidism, requiring lifelong calcium and vitamin D supplementation, significantly impacting their quality of life. Hypocalcemia resulting from hypoparathyroidism increases neuromuscular excitability, leading to symptoms like perioral numbness, peripheral paresthesia, and muscle cramps. Severe hypocalcemia can cause laryngeal spasms, tetany, seizures, and potentially life-threatening cardiac complications [9,11]. Despite the surgical challenges, identifying and protecting parathyroid glands during surgery is crucial for safe treatment. Surgeons should aim to prevent postoperative hypoparathyroidism, recognize early parathyroid insufficiency, and plan appropriate pharmacotherapy to avoid symptomatic hypocalcemia, ensuring better patient well-being and comfort during recovery. The aim of this study has been to evaluate the incidence of hypoparathyroidism and clinical manifestations of hypocalcemia after total thyroidectomy.

Methodology & Materials

This is a retrospective study, a total of 350 patients were enrolled and analyzed in this study. The study was conducted at the Department of General Surgery in four different Hospital, (Prime Hospital, American Hospital, NMC Hospital and Gladstone hospital; though it is a multi-center study), in different parts of the world. The study spanned two years,

from 2020 to 2022, during which a total of 820 thyroid gland surgical operations were conducted, including 350 total thyroidectomies. The focus of the study was on postoperative hypoparathyroidism, specifically as an early complication of surgery. However, the investigation did not extend to determining this complication's temporary or permanent nature in the longer perspective. Before data collection, explicit informed consent was obtained from each participant, and stringent measures were in place to ensure the data's confidentiality.

Inclusion criteria:

- Patients under the age group of 18 to 85 years.
- Individuals who have undergone a complete thyroidectomy.
- Absence of hypoparathyroidism in the patient's medical background.
- Assessment of parathyroid hormone (PTH) concentration within the initial 24 hours post-surgery.

Exclusion criteria:

- Individuals with additional coexisting medical conditions.
- Pregnant women.

Postoperative hypoparathyroidism was diagnosed by assessing low levels of serum calcium and parathyroid hormone (PTH). Given the short half-life of PTH in circulation, ranging from 2 to 4 minutes, measuring PTH levels serves as an effective early diagnostic approach for postoperative hypoparathyroidism (Singh et al. 2013). The information was organized systematically into tables or graphs based on their relevance. Detailed descriptions accompanied each table and graph to ensure a clear understanding. Statistical analysis was conducted using the Statistical Package for Social Science (SPSS) program on the Windows platform. Continuous parameters were transformed into categorical parameters and presented as frequency and percentage for clarity.

Result

Table 1 shows the age distribution of the study population; most of the 144(41.14%) patients were from the age range 65-60 years, second most 101(28.86%) patients were aged more than 60 years, and 30.00% of the study population were from the age group 18-45 years. Females dominate the cohort with 86.00%, while males account for 14.00% (Figure 1).

Age range (in years)	Frequency (n)	Percentage (%)
18-45 years	105	30.00
45-60 years	144	41.14
>60 years	101	28.86
Total	350	100.00

Table 1: Age distribution of the study population (N=350).

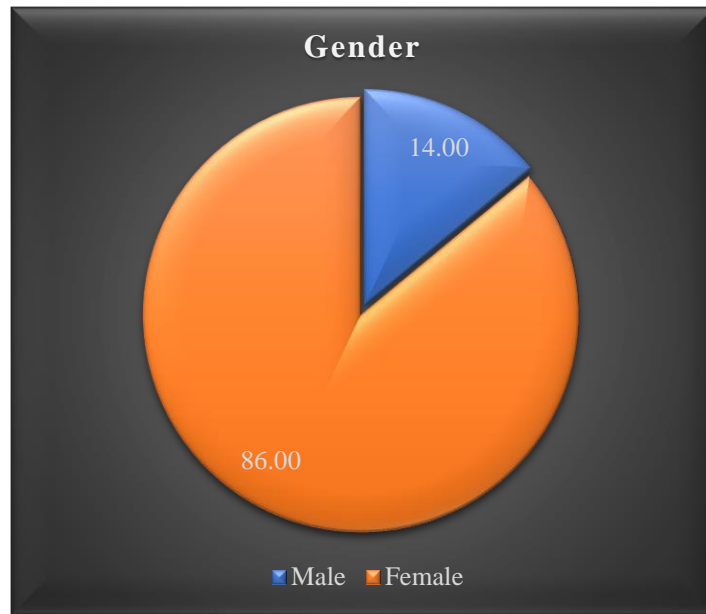


Figure 1: Gender distribution of the study population (N=350).

The majority (87.14%) underwent total thyroidectomy without lymphadenectomy, while a smaller proportion (12.86%) had the procedure with lymphadenectomy (Figure 2).

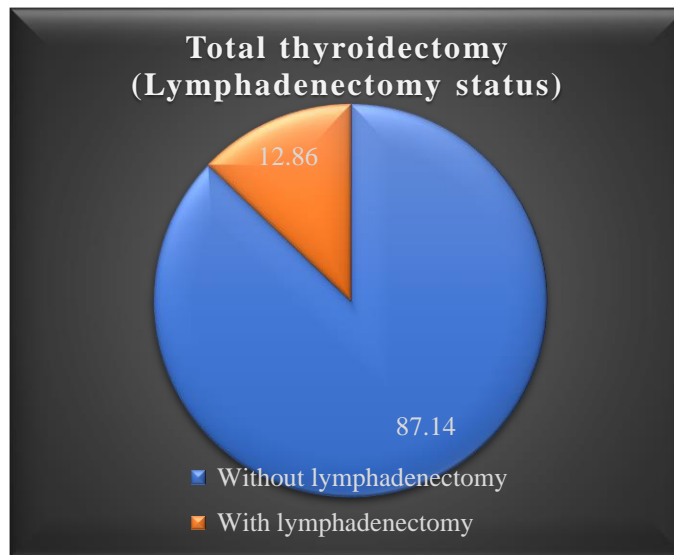


Figure 2: Types of surgical procedures performed in the studied group (total thyroidectomies).

Histopathological diagnoses	Frequency (n)	Percentage (%)
Thyroid cancers		
Papillary thyroid carcinoma	36	10.29
Follicular thyroid carcinoma	4	1.14
Medullary thyroid carcinoma	2	0.57
Anaplastic thyroid carcinoma	1	0.29
Metastasis of claro-cellular carcinoma to the thyroid gland	2	0.57
Nodular goiter		
Non-toxic nodular goiter	199	56.86
The nodular variant of Hashimoto's disease	2	0.57
Nodular goiter with morphological features of hyperactivity	92	26.29
The nodular variant of Graves' disease	12	3.43

Table 2: Histopathological diagnoses of the study population (N=350).

Table 2 outlines the histopathological diagnoses in the study population where Thyroid cancers, predominantly papillary thyroid carcinoma (10.29%), form a notable subset. However, Non-toxic nodular goiter dominates at 56.86%, indicating a prevalent benign thyroid condition, and hyperactivity features (26.29%) emphasize the complexity of thyroid pathology. In total thyroidectomy without lymphadenectomy, 46.86%

exhibit PTH levels below 15.0 pg/ml, indicating potential hypoparathyroidism. Conversely, in total thyroidectomy with lymphadenectomy, a majority (58.00%) has PTH levels below 15.0 pg/ml, suggesting a potential impact on parathyroid function due to more extensive surgery (Table 3).

Serum PTH level	Total thyroidectomy without lymphadenectomy		Total thyroidectomy with lymphadenectomy	
	n	%	n	%
0-14.99 pg/ml	164	46.86	203	58.00
≥15.0 pg/ml	186	53.14	147	42.00

Table 3: Serum PTH concentrations depending on the extent of surgery.

Variables	Decreased PTH level		Normal PTH level	
	n	%	n	%
Lymphadenectomy	201	57.43	149	42.57
Graves' disease	224	64.00	126	36.00
Recurrent goiter	200	57.14	150	42.86
Intraoperative hemorrhage/reoperation because of hemorrhage	210	60.00	140	40.00
Huge retrosternal goiter	197	56.29	153	43.71
Thyroidectomies without additional risk factors	157	44.86	193	55.14

Table 4: Variation in serum PTH levels, either reduced or within the normal range, is influenced by factors that elevate the likelihood of postoperative hypoparathyroidism.

According to Table 4, instances of lymphadenectomy, Graves' disease, recurrent goiter, intraoperative hemorrhage, and huge retrosternal goiter show a higher incidence of decreased PTH levels, ranging from 57.43% to 64.00%. In contrast, thyroidectomies without additional risk factors demonstrate a lower prevalence of decreased PTH levels at 44.86%. The

contrast in normal PTH levels is evident, with thyroidectomies without added risk factors exhibiting a higher percentage (55.14%), while cases with risk factors show lower percentages ranging from 36.00% to 43.71%. In Table 5,

Number of parathyroid glands	Serum PTH level			
	0-14.99 pg/ml (n=212)		≥15 pg/ml (n=138)	
	n	%	n	%
No gland	77	45.56	97	70.29
1	130	76.92	41	29.71
2	5	2.96	0	0.00

Table 5: The levels of parathyroid hormone (PTH) in serum vary based on the quantity of parathyroid glands identified in histopathological specimens.

when no glands are identified, most exhibit PTH levels in the lower range (0-14.99 pg/ml) at 45.56%, while 70.29% of cases with PTH levels ≥15 pg/ml have no identified glands. Conversely, when one gland is identified, a higher percentage (76.92%) demonstrates PTH levels in the lower range, and when two glands are identified, all 5 cases (2.96%) have PTH levels in the lower range. This suggests a potential association between the quantity of identified parathyroid glands and serum PTH levels.

Discussion

Hypoparathyroidism resulting from thyroidectomy worsens quality of patients' life because of the necessity of chronic pharmacological treatment and medical care. Most frequently, postoperative hypoparathyroidism is not a result of permanent destruction of parathyroid glands and usually it persists during 6 months (sometimes 1-2 years) after surgery. When patients treated because of persistent postoperative hypoparathyroidism were reevaluated after therapy withdrawal, it turned out that 2-5 years after surgery 50% of them did not need substitutive therapy (they had normal PTH and calcium levels) [12]. In this study, majority of 144(41.14%) patients were aged between 45-60 years and our male-female ratio is 1:6.34, which is similar to a study done by Marcinkowska in 2017 [13]. Another study done by Zobel et., al. 2020 found 16.18% male and 83.82% female [14]. In Marcinkowska's case-control study, he found 87% of cases of total thyroidectomy without

lymphadenectomy and 13% of cases were with lymphadenectomy [13]. This finding is almost same to our study. In this study, papillary thyroid carcinoma was common carcinoma in thyroid cancer and under nodular goiter, 56.86% of cases had non-toxic nodular goiter. In total thyroidectomy without lymphadenectomy, 46.86% exhibit PTH levels below 15.0 pg/ml, indicating potential hypoparathyroidism. Conversely, in total thyroidectomy with lymphadenectomy, a majority (58.00%) has PTH levels below 15.0 pg/ml, suggesting a potential impact on parathyroid function due to more extensive surgery. The frequency of postoperative hypoparathyroidism varies considerably between different surgical centers. Temporary hypoparathyroidism occurs in 1.6-50% patients, while permanent one in 1.5-4.9% cases [7, 15, 16]. In our study, postoperative hypoparathyroidism, based on serum PTH levels measured on the first day after total thyroidectomy, was recognized in 57.43% of patients with decreased PTH level and in 42.57% of patients with normal PTH levels symptoms of hypocalcemia were present. Many authors postulate that PTH determination is the most effective strategy to identify postoperative hypoparathyroidism, in contrary to other clinical and laboratory (e.g. serum calcium level) parameters. Measurement of serum PTH levels has the advantage of directly assessing gland function. There is a debate whether PTH measurements should be performed intraoperatively, few hours or one day after thyroidectomy [5,17,18]. In one of the recent studies, in which 806 total thyroidectomies were

analyzed, the overall incidence of hypocalcemia was 23.6%, with the permanent hypocalcemia in 1.61% and symptomatic hypocalcemia in 10.91% [19]. The intraoperative intact PTH assay which is recommended by Australian Society of Endocrine Surgeons is a good tool to predict postoperative hypocalcemia. The authors noted that this test has low sensitivity but high specificity [19]. In other study, Rivere et al. concluded that PTH assay in the blood samples collected in the morning after total thyroidectomy was an effective strategy to detect hypoparathyroidism [20]. The authors recommend an assessment of PTH concentration after total thyroidectomy and supplementation of calcium and calcitriol in patients with serum PTH levels ≤ 13 pg/ml to avoid symptomatic hypocalcemia and prolonged hospitalizations [20]. In prospective, randomized controlled study conducted by [21], PTH levels were also obtained in the morning after surgery and the authors concluded that it was highly specific method of prediction whether the patients were at risk of symptomatic hypocalcemia. They have established that PTH concentration below 10 pg/ml allows to accurately identify patients with high risk of hypocalcemia (48% had presented symptomatic hypocalcemia), whereas all patients with a postoperative PTH ≥ 10 pg/ml can safely be discharged from hospital without supplementation [21]. According to the correlation between the quantity of identified parathyroid glands in histopathological specimens and serum parathyroid hormone (PTH) levels. Notably, when no glands are identified, the majority exhibit PTH levels in the lower range (0-14.99 pg/ml) at 45.56%, while 70.29% of cases with PTH levels ≥ 15 pg/ml have no identified glands. Conversely, when one gland is identified, a higher percentage (76.92%) demonstrates PTH levels in the lower range, and when two glands are identified, all 5 cases (2.96%) have PTH levels in the lower range. This suggests a potential association between the quantity of identified parathyroid glands and serum PTH levels. These finding are same to another study done by Marcinkowska et., al. (2017) [14].

Limitations of the study: Despite the comprehensive exploration of postoperative hypoparathyroidism following total thyroidectomy in a multi-center study in India, several limitations need to be acknowledged. Firstly, the study's retrospective nature may introduce inherent biases and limit the establishment of causal relationships. Additionally, the investigation's focus on early complications does not provide insights into the long-term outcomes of hypoparathyroidism. The exclusion of individuals with coexisting medical conditions may limit the generalizability of findings to a broader patient population. Furthermore, the study's timeframe, spanning only two years, may not capture the evolving trends and variations in surgical practices. These constraints highlight the need for further prospective and extended-duration studies for a more comprehensive understanding of postoperative hypoparathyroidism in diverse patient cohorts.

Conclusion And Recommendations

In conclusion, this multicenter study highlights the significant incidence of postoperative hypoparathyroidism in patients undergoing total thyroidectomy. The study reveals a correlation between the extent of surgery, histopathological diagnoses, and the likelihood of decreased parathyroid hormone (PTH) levels. Factors such as lymphadenectomy, Graves' disease, recurrent goiter, intraoperative hemorrhage, and huge retrosternal goiter contribute to a higher incidence of decreased PTH levels, emphasizing the importance of careful consideration during surgery. To enhance patient outcomes, it is imperative to implement strategies for the early detection and management of postoperative hypoparathyroidism. Routine monitoring of serum PTH levels within the initial 24 hours post-surgery proves to be a valuable diagnostic approach. Surgeons should exercise caution in cases involving additional risk factors and consider tailored interventions to minimize the impact on parathyroid function. Recommendations include incorporating intraoperative intact PTH assays to predict and prevent symptomatic hypocalcemia, particularly in cases with identified risk factors.

Additionally, the study underscores the potential association between the quantity of identified parathyroid glands and serum PTH levels, warranting further investigation for a comprehensive understanding.

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