

Frequency and Risk Factors of Hypoparathyroidism after Total Thyroidectomy

Risk Factors of Hypoparathyroidism after Total Thyroidectomy

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ABSTRACT

Objective: To identify the frequency and risk factors of post-surgical hypoparathyroidism after total thyroidectomy.

Study Design: Randomized clinical study

Place and Duration of Study: This study was conducted at the Department of General Surgery, Jinnah Postgraduate Medical Centre Karachi from January 2020 to January 2021 for a period of one-year.

Materials and Methods: One hundred and sixty eight patients planned for total thyroidectomy were included. Frequency of hypoparathyroidism was noted at 6 months' follow-up. Risk factors of hypo-parathyroidism were determined by applying logistic regression.

Results: Transient hypoparathyroidism was seen more in carcinoma, thyroiditis and parathyroid disease patients, 44 (93.6%), 10 (21.2%) and 9 (19.1%) versus 94 (77.2%), 73 (60.2%) and 14 (11.57%, p-values 0.03, 0.048, and 0.001 respectively). Transient hypoparathyroidism seen more in lateral lymph node dissection patients including both central lymph node dissection and modified radical neck dissection, p= 0.002 and 0.03 respectively. Female gender was highly correlative with hypoparathyroidism with odds ratio OR= 2.246 (1.282–3.120, p=0.001), pathological condition of parathyroid gland OR= 1.620 (1.087–2.046, p=0.029) and extent of central lymph node dissection (bilateral) OR= 1.637 (0.081-2.231, p=0.018).

Conclusion: The independent risk factors for hypoparathyroidism after total thyroidectomy are; female gender, bilateral central lymph node dissection and extent of central lymph node dissection, pre-operative parathyroid gland pathology and malignancy.

Key Words: Hypothyroidism, Total thyroidectomy, Risk factors, Frequency

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INTRODUCTION

Hypoparathyroidism is one of the rare endocrine hormone deficiency diseases. The etiology of parathyroid deficiency due to genetic abnormality, consider as primary hypoparathyroidism, acquired or secondary hypoparathyroidism occurs due to ablate, extinguish, or functional impairment of parathyroid gland.¹ Secondary hypoparathyroidism is the most common character.

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Though, the diagnosis pattern is made by low serum calcium (Ca) levels, increased level of phosphorus, and abnormally low level of parathyroid hormone (PTH) in the blood circulation.² In the united states of America, the estimated prevalence rate of hypoparathyroidisms around 37 out of 100000 persons per year.³

Thyroidectomy surgery can be performed when thyroid cancer or goiter disease is identified. Post-surgery hypoparathyroidism is a regular complication resulting from total thyroidectomy. Hypoparathyroidism lasting less than 6 months (transient hypocalcemia) found in 25.4-83%, and 0.12-4.6% have lasting more than 6 months (permanent hypocalcemia).⁴ Surgical injury, vascular compromise, and unintentional removal of the parathyroid gland are the primary causes of post thyroidectomy hypocalcemia. The type of surgical intervention and surgical expertise varies from center to center in secondary hypoparathyroidism. Worldwide, the prevalence rate of postsurgical hypoparathyroidism in 22 out of 100,000 patients.⁵

In post-operative period after total thyroidectomy, symptoms of hypocalcemia can be treated with calcium (Ca) supplementation abnormal level of hypocalcemia increases the patient's stay in the hospital, which is a financial burden to the hospital.

Though surgeons are concerned about hypocalcemia prediction and start treating early to avoid post-op complications as well as delay in discharge from the hospital. Patients pathological and clinical conditions and various dissection techniques might predict the hypocalcemia in post-surgical period.⁵ Serum calcium values monitoring is a traditional method, even though absolute Ca values cannot sufficient to predict its development.⁶ Some studies reported that intact parathyroid hormone (iPTH) values are important to predict the hypocalcemia post thyroidectomy but the drawback of iPTH is cost-effective and lacks convenience.⁷⁻¹⁰

Our present study goal was to identify the frequency and risk factors of post-surgical hypoparathyroidism after total thyroidectomy.

MATERIALS AND METHODS

In this randomized clinical study, we included 168 patients from the Department of General Surgery, Jinnah Postgraduate Medical Centre Karachi from 1st January 2020 to 1st January 2021. All patients planned for total thyroidectomy, male and female patients, age 18-60 years were included. All patients having renal disorders associated parathyroid disease, history of neck and thyroid surgery and who were unable to understand verbal and written commands were excluded.

After approval of the research proposal from the ethical review committee of the hospital, we included 168 patients who were scheduled for total thyroidectomy. Written informed consent was taken from all patients before including in this study and thoroughly explaining to them the outcomes of the study. Data regarding the patient's age, gender, body mass index (BMI), hormonal status, Ca and phosphorus was recorded. During surgery, we noted the tumor size, operation time, need of lymph node dissection (LND), central neck dissection (CND), and modified radical neck dissection (MRND) and the underlying pathological condition was also included.

Data analysis was carried out by SPSS-23, quantitative variables were calculated as mean±SD, to compare these variables between the normal and transient hypoparathyroid group an independent sample t-test was applied. For qualitative variables frequency was calculated and Logistic regression was used to describe data and to explain the relationship between hypoparathyroidism and calcium dependency. Statistical P-value <0.05 indicated as significant.

RESULTS

There were 121 normal and 47 transient hypoparathyroidism patients identified. The mean age of the normal group was 52.2±3.25 years and 49.65±2.84 years in transient hypoparathyroidism (p-value < 0.0001). There were 145 (86.3%) females and

23 (13.7%) males. In comparison with males, transient hypothyroidism was significantly (p-value <0.0001) seen more in female patients, transient hypothyroidism was found in 4 (8.51%) males and 42 (89.3%) in female patients. Transient hypoparathyroidism was seen more in carcinoma, thyroiditis and Parathyroid disease patients, 44 (93.6%), 10 (21.2%) and 9 (19.1%) versus 94 (77.2%), 73 (60.2%) and 14 (11.57%, p-values 0.03, 0.048 and 0.001) respectively. Transient hypoparathyroidism seen more in LND patients; including both CND and MRND, p=0.002 and 0.03 respectively (Table 1).

All the parameters statistically analyzed following logistic regression to identify the correlation with hypocalcemia and based on that odds ratio was calculated. Female gender was highly correlative with hypoparathyroidism with odds ratio OR= 2.246 (1.282–3.120, p-value 0.001), pathological condition of parathyroid gland OR= 1.620 [1.087–2.046, p-value=0.029) and extent of CND (bilateral) OR=1.637 (0.081–2.231, p-value 0.018). These three parameters were statistically significant in evolving hypocalcemia in transient patients (Tables 2-3).

Table No.1: Basic characteristic and pathological condition developing in hypocalcemia (n=168)

Parameter	Normal (n=121)	Transient hypothyroidism (n=47)	P value
Age (years)	52.2±3.25	49.65±2.84	< 0.0001
BMI (kg/m ²)	24.76±4.94	25.32± 3.28	0.47
Gender			
Male	18(14.8%)	5 (10.6%)	<0.0001
Female	103(85.12%)	42 (89.4%)	
Underlying pathology			
Carcinoma	94 (77.2%)	44 (93.6%)	0.03
Thyroiditis	73 (60.2%)	10 (21.2%)	0.048
Parathyroid present	14 (11.57%)	9 (19.1%)	0.001
LN dissection			
CND	95 (78.5%)	40 (85.1%)	0.002
MRND	9 (7.4%)	6 (12.76%)	0.03
Tumor size	3.6±4.4	4.2±5.4	0.45
Hormonal status			
Hypothyroid	13 (10.74%)	5 (10.63%)	0.39
Hyperthyroid	5 (4.1%)	3 (6.38%)	0.12
Calcium (mg/dl)	9.1±2.2	9.4±2.6	0.45
Phosphorous (mg/dl)	3.6±1.2	3.8±1.3	0.34
Surgery time (min)	149.1±42.4	155.6±50.2	0.39

Table No.2: Risk Factors of hypoparathyroidism based on Logistic regression

Variable	P-value	Odds ratio (CI)
Age	0.082	0.942 [0.910–1.021]
Gender(Female)	0.001	2.246 [1.282–3.120]
CND	0.631	1.143 [0.986–1.842]
MRND	0.054	1.162 [0.930–2.932]
Extent of CND (bilateral)	0.018	1.637 [0.081–2.231]
Operation time	0.312	0.983 [0.904–1.081]
Parathyroid gland in pathology	0.029	1.620 [1.087–2.046]

Table No.3: Hypoparathyroidism prevalence at different stages

Hypothyroidism stages	N=168	Prevalence	95% CI
At hospital discharge	72	42.8%	41.3 – 46.8
After 3 months follow-up	47	27.9%	24.2 – 29.8
After 6 months follow up	24	14.2%	12.8 – 15.8
Early recovery (transient)	39	23.2%	20.6 – 26.4

DISCUSSION

Hypoparathyroidism development in total thyroidectomy cannot be linked with a single risk factor, different studies have been conducted on various factors prone to hypoparathyroidism. Independent factors identifying is not an easy task. Different morbidities related to hypoparathyroidism are directly associated with hypocalcemia or hyperphosphatemia, indirectly deficient amount of Ca, and inactive vitamin D. When treatment is altered, due to hypercalcemia, neuromuscular excitability occurs then symptoms persist and hypercalciuria occurs when excessive Ca and vitamin D intake. Complications of hypoparathyroidism can cause ectopic calcification that happens in the gray-white matter and basal ganglia interface in the brain, decreased skeleton remodelling, and subcapsular cataracts are other complications related to hypoparathyroidism.

According to a study conducted post thyroidectomy approximately 33% of patients become hypoparathyroidism due to malignant diseases., 33% due to non-toxic goiter surgery, 10% due to primary hyperparathyroidism, and 25% due to toxic goiter.¹¹

In the present study, there were 4 males and 42 females identified as transient hypoparathyroidism. The female gender shows a high frequency of hypoparathyroidism

compares to males for postoperative hypocalcemia. Odds ratio = 2.246 [1.282–3.120] at 95% CI. Cho et al², the same kind of study conducted on 1030 patients, they described, the female gender is highest hazard ratio for hypoparathyroidism with (HR=2.285; 95% confidence interval = 1.391–3.751). Previous studies have the same concept on female gender prevalence.^{12, 13} Because female diseases are linked to various hormones, indirectly interact with Ca or vitamin D. in this study due to limitation we did not include vitamin-D measurement.

In our study center, two-third of the surgical patients who underwent surgery due to carcinoma 94(77.2%). We found most of them proven for transient hypoparathyroidism. According to Page et al⁴ and Shoback¹⁴ study, transient hypoparathyroidism range between 6.9-46% after the thyroidectomy surgery. In LND surgery parathyroid dysfunction lasts long up to one year.¹⁵ Surgery for graves' disease and anterior neck involving shown a high risk for postoperative hypoparathyroidism.

In post-operative patient, the calcium level found 9.4±2.6 mg/dl (transient), which almost mimic to the Ansari et al study¹⁶, in their 170 patient total thyroidectomy study, they documented post-surgical calcium levels of <8.6mg/dl without symptoms and 2nd postoperative day it was 9.4 mg /dl with neuromuscular symptoms. after the total thyroidectomy, there was autoimmune hypoparathyroidism is most commonly occurs in an adult.¹⁷

Central lymph node dissection, MRND and extend of thyroidectomy are regular consider for the hypocalcemia.^{18, 19} In our regression analysis malignancy, extend of bilateral CND was significantly associated with hypocalcemia. There was a controversial concept regarding the increase in surgical operating time directly caused by hypocalcemia. In our study, we have observed those who had longer surgical time, they developed hypocalcemia postoperatively. In our study, those patients having parathyroid pathology had a significantly high prevalence of hypocalcemia (Odds ratio = 1.620[1.087–2.046]).

The present study showed that a decrease in Ca and an increase in phosphorus levels were found on the first and the second postoperative days. Hypoparathyroidism prevalence has been gradually decreased at different stage periods (Table 3).

The limitation of this study was only a six months follow-up transient hypoparathyroidism study; we did not follow patients for a longer period. The study sample size was small, for fine results there is a need to conduct the study at a large center where a high volume of total thyroidectomy doing and document the long-term follow-up.

CONCLUSION

The independent risk factors for hypoparathyroidism after total thyroidectomy are; female gender, bilateral CND and extent of CND, pre-operative parathyroid

gland pathology, and malignancy. Known of the above high-risk factor patient going to thyroidectomy surgery, care should be taken to preserve the parathyroid function during surgery. Special postoperative care has to be taken to prevent the risk of hypoparathyroidism by monitoring Ca and phosphorous levels.

Author's Contribution:

Concept & Design of Study: Rizwan Khan
 Drafting: Anila Ahmed, Nazia Khatoon
 Data Analysis: Sobia Majeed, Sumta Khan
 Revisiting Critically: Rizwan Khan, Anila Ahmed
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