

# Low Parathormone Level Following Total Thyroidectomy- Observation of Patient Traits in A Single Institute

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## ABSTRACT

**Objective:** Surgical debulking of thyroid and neck lymph nodes is the mainstay of differentiated thyroid cancer treatment, during which parathyroid glands are at risk of either removal or vascular insufficiency. The purpose of this study was to evaluate and categorize the total thyroidectomy patients with low parathormone (PTH) levels who were referred for radio-iodine ablation therapy.

**Patients and Methods:** Two hundred seventeen differentiated thyroid cancer (DTC) patients who underwent total thyroidectomy with or without modified neck dissection between February 2020 and December 2022 were evaluated retrospectively. This was a simple observational study. Post-operative levels of serum PTH and calcium were documented, and statistical analysis was performed.

**Results:** Among 217 patients, post-operative low PTH levels were observed in 51.2% and low serum calcium in 27.6% of total patients. Moreover, 50.7% of total thyroidectomy patients and 52.1% of total thyroidectomy patients with modified neck dissection developed low parathyroid hormone levels. The age group most affected by low PTH levels was 25–34 years old. Furthermore, low serum calcium levels were found in 55% of patients who had a low PTH level.

**Conclusion:** In this study, the 25–34-year-old age group was more likely to develop a post-operatively low PTH level with female sex predilection.

**Keywords:** Parathyroid hormone, Serum calcium, Total thyroidectomy, Modified neck dissection.

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## INTRODUCTION

The management of thyroid cancer usually consists of surgical resection followed by medical treatment and regular

follow-up. (1) Differentiated thyroid cancers (DTC, including papillary and follicular adenocarcinomas) are around 90 percent of all thyroid malignancies. The initial treatment for DTCs is to remove the primary tumor and involved cervical lymph nodes. It significantly helps postoperative treatment with radioactive iodine and reduces the risk of recurrence and metastatic spread. Surgical treatment of the thyroid gland ranges from lobectomy to total thyroidectomy (complete removal of both lobes of the gland, the isthmus, and the pyramidal lobe).

In DTC, nodal metastasis at level VI is treated with a central (level VI) neck dissection. If nodes are suspicious in the lateral neck, then a selective neck dissection for levels II a–V b with preservation of the spinal accessory nerve (SAN), internal jugular vein (IJV), and sternocleidomastoid muscle (SCM) should be done. If the nodal disease involves surrounding structures such as the IJV, SCM, or skin, then these should also be excised during the lateral neck dissection.

Hypocalcaemia and hypoparathyroidism are the most common complications of thyroid surgery. (2) A mildly low PTH level is common after surgery but usually resolves within weeks. But permanent hypoparathyroidism can be a real clinical problem for total thyroidectomy patients. (3) Permanent hypoparathyroidism has been documented in patients undergoing a total thyroidectomy. (2) There is a risk of injury to the parathyroid glands during a total thyroidectomy, even in experienced surgical hands. (3) The

probability of parathyroid gland injury in neck dissection is mainly due to variable locations, delicate vascular supply, accidental removal, and the extent of dissection. (2) Total thyroidectomy causes temporary and permanent hypocalcemia in many patients. (4) Usually, differentiated thyroid cancer patients are referred to Nuclear Medicine institutes after total thyroidectomy for radio-iodine ablation therapy after 2-3 weeks of surgery. The main objective of this study was to evaluate and categorize the low PTH-level patients after total thyroidectomy with or without neck dissection who were referred to Institute of Nuclear Medicine and Allied Sciences (INMAS), Khulna.

### PATIENTS AND METHODS

An observational descriptive study was performed at the Institute of Nuclear Medicine and Allied Sciences, Khulna, from February 2020 to December 2022. Two hundred seventeen diagnosed differentiated thyroid cancer (DTC) patients who underwent total thyroidectomy with or without modified neck dissection and were also referred for radioiodine ablation were enrolled in the study. A proper history was taken from all patients according to the data collection sheet. The prospectively collected data were evaluated retrospectively. Patients having total thyroidectomy or completion thyroidectomy with or without central neck dissection were categorized into one group (those patients without lateral neck dissection were classified as the total thyroidectomy group). Total thyroidectomy with lateral neck dissection patients were categorized in another group (classified as a modified neck dissection group). Serum PTH level and calcium level were measured as routine baseline investigations by chemiluminescence assays and biochemistry analyzers, respectively, within weeks of surgery. The normal range of PTH level and serum calcium were defined as 18.5-88.0 pg/ml and 8.5-10.5 mg/dl, respectively. Low serum PTH and calcium level were considered as  $< 18.5$  pg/ml and  $< 8.5$  mg/dl respectively. Statistical analyses of quantitative data were done using Statistical Package for the Social Sciences (SPSS) version 25.0 for Windows. Variables are shown in number, mean, percentage, and  $\pm$ standard deviation. For all the variables, a chi-squared test was applied, and a P value  $< 0.05$  was considered statistically significant. Patients with high serum PTH levels, 2/19/24, DTCs unfit for operation, or locally advanced diseases were excluded.

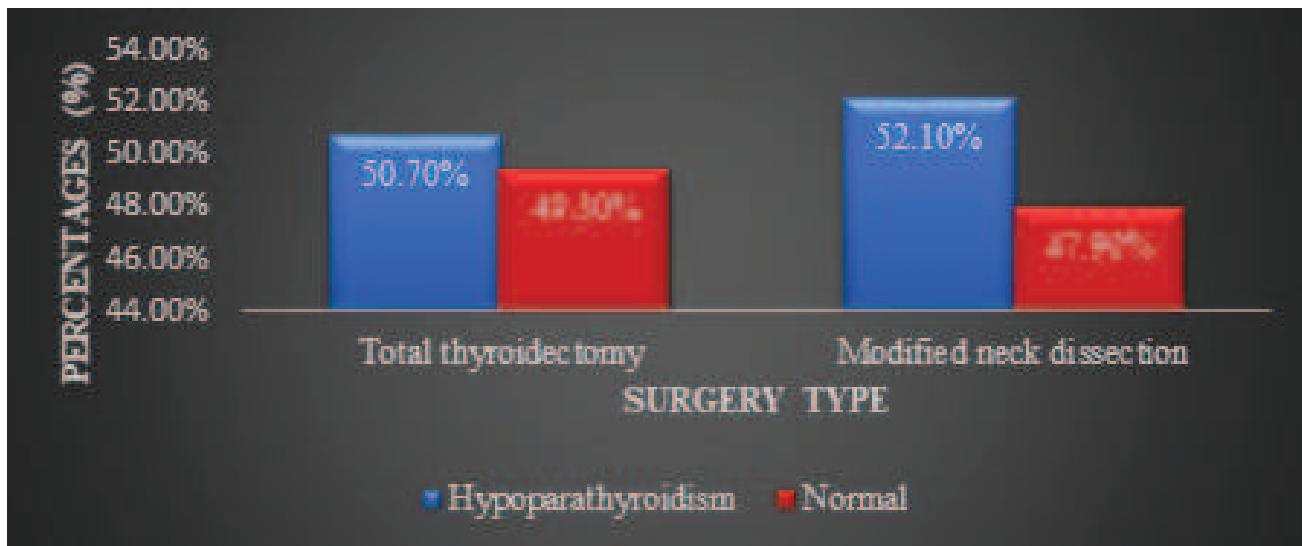
### RESULT

Among 217 patients, 183 were female (84.3%) and 34 were male (15.7%). Their age ranged from 15 to 72 years. Among those, 144 (66.4%) underwent total thyroidectomy and 73 (33.6%) underwent total thyroidectomy with modified neck dissection. Among 217, post-operatively low PTH levels were observed in 111 patients (51.2%). Among 111 patients, the 25–34-year-old age group (45–50% of total patients in this age group) suffered most from low PTH levels. Among the low PTH level group, 16 were male (47.1% of total male) and 95 were female (51.9% of total female) patients.

**Table 1: Serum parathormone status of study subjects (n=217) with demographic and biochemical difference between the patients of low and normal parathormone level.**

Variables	Low parathormone group(n%)	Normal parathormone group(n%)
<b>Total</b>	111(51.2)	106(48.8)
<b>Age</b>		
15-24	11(40.7)	16(59.3)
25-34	45(50)	45(50)
35-44	38(59.4)	26(40.6)
45-54	10(50)	10(50)
55-64	6(54.5)	5(45.5)
65+	1(20)	4(80)
<b>Gender</b>		
Male	16(47.1)	18(52.9)
Female	95(51.9)	88(48.1)
<b>Surgery Type</b>		
Total thyroidectomy	73(50.7)	71(49.3)
Modified neck dissection	38(52.1)	35(47.9)
<b>Serum Calcium</b>		
Hypo	33(55)	27(45)
Normal	78(49.7)	79(50.3)

Moreover, among 111 patients, 73 patients (50.7% of 144) had total thyroidectomy, and 38 patients (52.1% of 73) had total thyroidectomy with modified neck dissection and developed low parathormone levels. The mean serum PTH level was  $7.627 \pm 5.648$  ( $\pm$  SD) in the low PTH level group. Low serum calcium levels were found in 60 patients (27.6% of total patients) and 33 patients (55%) among patients with low PTH levels. None of the variables in this study are significantly predicting the outcome.



**Figure 1: Postsurgical biochemical status of the study subjects with type of surgery.**

**DISCUSSION**

Complications are often unavoidable after a total thyroidectomy, which may be temporary or permanent. Complications can be divided into early, intermediate, and late. Early complications following thyroidectomy include haemorrhage, voice change, airway obstruction and temporary hypoparathyroidism. The intermediate complications are seroma formation, infection, and temporary palsy of the recurrent laryngeal nerve (RLN) and the external branch of the superior laryngeal nerve. Late complications comprise subclinical hypothyroidism, permanent hypoparathyroidism, permanent injury to the recurrent laryngeal nerve, the superior laryngeal nerve, the cutaneous nerves, and the accessory nerve, and poor scar formation (2).

Postoperative hypoparathyroidism is a major, often severe complication after surgery. In our study, we measured serum PTH within a few days to weeks of surgery. The diagnosis of postoperative hypoparathyroidism can be performed on the basis of low serum calcium and PTH levels as well as clinical symptoms of hypocalcaemia. The half-life of PTH in circulation is 2–4 minutes, so PTH measurement can be used as an early diagnostic method of postoperative hypoparathyroidism (5). Controversy exists regarding the best time for their determination in predicting postoperative transient or permanent hypoparathyroidism. More recently, intact PTH (iPTH) levels at intraoperative, perioperative, or in the immediate postoperative period have been

recommended to evaluate hypoparathyroidism more clearly. Asari et. al. stated that on the first two postoperative days, interpretation of iPTH levels as well as sCa levels seems like an optimal strategy for predicting patients at risk of hypoparathyroidism (6).

In our study, about half of the patients (51.2%) developed a temporary low PTH level within weeks of surgery. Masanori et. al. and Ismail et. al. stated that post-operative transient hypoparathyroidism was observed in 68% of 65 patients and 20.3% of 542 patients having total thyroidectomy with neck dissection for thyroid cancer, respectively (7, 8). This difference in percentage may be due to a small study group or a different time of sample collection, as we measured serum PTH within a few days to weeks of surgery. It is the limitation of our study that we had no data regarding perioperative serum PTH and sCa levels. Most patients with thyroid problems are usually treated in smaller surgical units in our country. Therefore, monitoring intraoperative iPTH levels may be tough and increase the cost of the treatment in our clinical setting.

Controversy exists over the associated factors of postoperative transient or permanent hypoparathyroidism. Among 111 patients, 25–34-year-olds and females suffered most from low PTH levels. Marcinkowska et. al. showed that they did not find any influence of age on the incidence of low PTH after thyroid surgery (5). Moreover, among the 111 patients, 50.7% had total thyroidectomy and 52.1% had total thyroidectomy with modified neck dissection and

developed a low PTH level. Ritter et. al. showed that low PTH levels were not associated with age, sex, or neck dissection. (9) However, Teshima et. al. stated that transient hypoparathyroidism may have increased incidence in the female group and the extent of surgery (7). Again, Marcinkowska et. al. stated that the highest risk of hypoparathyroidism occurred in patients in whom total thyroidectomy was widened by lymphadenectomy and the lowest in patients who underwent lobectomy (5). In another study, Yong Sang Lee et. al. also showed that there was an increased incidence of transient hypoparathyroidism in lateral neck or modified neck dissection compared to total thyroidectomy with central neck dissection (10). In our study, we hadn't found any statistical differences with sex, age, or extent of surgery.

Hypocalcaemia leads to neuromuscular excitability, facial numbness, paraesthesia, and muscle cramps. Laryngeal spasm, tetany, seizures, and cardiac symptoms are serious and potentially life-threatening complications of severe hypocalcaemia (5). Decreased serum calcium (sCa) levels measured on the first postoperative day were often observed. This phenomenon has usually been debated, as it can often be explained by hemodynamics after surgery. However, decreasing sCa levels may decline up to the first three postoperative days due to it. The sensitivity of sCa measurements can decline on the fourth postoperative day. It may be due to the fact that some patients receive calcium and calcitriol therapy during the third and fourth days. Monitoring of intraoperative iPTH levels could predict whether patients need intravenous calcium therapy or not during the first postoperative day. However, practically, it is needed for a few patients (6). In our study, transient hypocalcaemia was found in 27.6% of total patients and 55% of patients with low PTH levels. None of the variables are significantly predicting the outcome. However, it should be followed up in the long term to exclude permanent hypocalcaemia. Surgeons should not only prevent postoperative low PTH levels but also determine the drug treatments to avoid hypocalcaemia (5). Routine postoperative calcium and vitamin D supplementation may decrease the incidence of temporary hypocalcaemia (11). However, it may worsen the patients' quality of life because of the chronic drug therapy (5). When patients were treated due to persistent postoperative low PTH levels and

re-examined after therapy withdrawal, it turned out that 2–5 years after surgery, 50% of them did not actually need this therapy (9).

It was a single center-based study. So, institutional bias might be an obstacle to our study. Intra-operative auto-transplantation of parathyroid (two or more) glands may prevent post-operative hypoparathyroidism (7). In patients undergoing parathyroid auto-transplantation, it is not clear whether the transplant itself, the parathyroids left in situ, or possible supernumerary glands provide sufficient parathyroid function to maintain sCa levels postoperatively (6). Most frequently, postoperative hypoparathyroidism is not a result of the permanent destruction of parathyroid glands. As it usually persists for about 6 months to 6 months (sometimes 1–2 years) after surgery, it can be termed parathyroid insufficiency (5, 6). In our study, patients had not been followed up in the long term to exclude permanent hypoparathyroidism. So, we need to add follow-up of PTH as well as serum calcium at 6 months, 1 year, and 2 years within our treatment protocol.

## CONCLUSION

Performing a total thyroidectomy with modified neck dissection may not significantly increase the risk of developing a low PTH level compared to patients having a total thyroidectomy for differentiated thyroid cancer. Patients with low PTH as well as low calcium levels are of greater concern. However, these patients should be followed up after 6 months to 1 year for screening for permanent hypoparathyroidism followed by permanent hypocalcaemia.

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