

Original Research Article

Early hypocalcemia following thyroidectomy in Kurmitola General Hospital, Dhaka, Bangladesh

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ABSTRACT

Background: Hypocalcaemia is a recognized complication after thyroidectomy, which may be transient or permanent due to impairment of blood supply, injury, or inadvertent removal of the parathyroid gland. Parathormone, secreted by parathyroid gland, plays an important role in calcium homeostasis. Purpose of this study was to enable early detection of hypocalcaemia after thyroidectomy, aiding in patient management, early discharge, and reduced hospital stay.

Methods: This study was conducted in the otolaryngology and head-neck surgery department of Kurmitola General Hospital over 12 months, from January 2020 to December 2020. Patients with various indications were selected based on eligibility criteria through convenience sampling. Data were collected using a data collection sheet, then cleaned, edited, and tabulated. The results were analyzed using the student's unpaired t-test (quantitative data) to determine their significance, with a p cut-off set at <0.05.

Results: Data analysis of 30 patients (30% male, 70% female) revealed that 13 patients experienced hypocalcaemia, while 17 showed normocalcaemia. Among the 13 hypocalcaemic patients, 10 (76.92%) had asymptomatic (subclinical) hypocalcaemia, and 3 (23.08%) had symptomatic hypocalcaemia. Hypocalcaemia was observed in 46.15% of patients within 24 hours post-surgery, 38.46% within 48 hours, and 15.39% within 72 hours. The results indicated a female predominance in the development of hypocalcaemia.

Conclusions: The study suggests that serum calcium levels significantly decrease after total thyroidectomy, with most cases occurring within 48-72 hours post-surgery.

Keywords: Hypocalcaemia, Total thyroidectomy, Normocalcaemia, Parathormone

INTRODUCTION

Thyroid surgery is one of the most common surgeries in the world. It is the definitive management option for

thyroid malignancies, and also for benign diseases such as multinodular goitre with compression symptoms and, the consequent early hypocalcaemia is its frequent complication. Hypocalcaemia may be permanent or

transient. It may happen in case of thyroid surgery in the hands of very expert surgeons too. Majority of the cases of hypocalcaemia usually develops 24 to 72 hours after the thyroidectomy. The transient hypocalcaemia may be asymptomatic (subclinical) or symptomatic which improves with calcium supplement and becomes normocalcaemic within 2 to 3 months. Up to 30% incidence of postoperative asymptomatic transient hypocalcaemia on first postoperative day and 6% of temporary hypocalcaemia necessitate calcium supplement.¹

Very few patients (1%-3%) may develop postoperative permanent hypocalcaemia following total thyroidectomy.¹ The risk of permanent hypoparathyroidism following thyroidectomy varies from 0 to 10%.² Incidence of permanent hypocalcaemia reported in different studies are 0.7%, 5%, 5.4% and 7.7%.³⁻⁶ In one study permanent hypocalcaemia was found in 16.77% patients.⁷ Hypocalcaemia following thyroid surgery should be considered permanent in those patients who continue to require calcium supplement after six months of surgery. Symptomatic patients often require extended hospitalization following thyroid surgery, leading to increased healthcare costs. Hypocalcaemia may occur in approximately 6% of cases after extensive thyroid surgery.⁸ This has been considered a serious concern because it may be potentially dangerous morbid condition as well as life threatening consequences.

Depending on the extent of parathyroid gland damage, hypocalcaemia may be transient, resolving within a few months, or permanent. Particularly with ambulatory thyroid surgery, which allows early discharge of patients, postoperative hypocalcaemia is an important consideration. In fact, some surgeons advocate indiscriminate postoperative calcium supplementation, though this approach has been contested.⁹ The interest in outpatient and short-stay thyroid surgery makes it especially helpful for surgeons to be able to identify patients at risk of developing hypocalcaemia. Among the thyroid surgery, total thyroidectomy is the most commonly practiced procedure for different indications. Total thyroidectomy is a demandable surgery for both malignant and benign thyroid disorders. This surgery is currently preferred treatment for thyroid cancer, multinodular goitre and Grave's disease and among patients with increased risk of recurrence.

The pathogenesis of hypocalcaemia is still not completely understood. But it can be assumed that there are multidimensional risk factors such as anatomical, biochemical, pathological, surgical and demographic. Hypocalcaemia after total thyroidectomy has been the most attributed to parathyroid insufficiency related to injury, devascularization, or inadvertent excision of the parathyroid glands. Hypoparathyroidism is an additional event whereas hypocalcaemia is relatively common after total thyroidectomy. The occurrence of such

complications has been attributed to the surgical techniques, reoperations, neck dissection and experience of the surgical team.

Some of the causative mechanisms linked to post thyroidectomy hypocalcaemia include: increased calcium uptake by the bone due to the postoperative reversal of thyrotoxic osteodystrophy (hungry bone) in patients with thyrotoxicosis, reactive hypoparathyroidism due to relative hypercalcaemia in thyrotoxic patients, where parathyroid suppression occurs from increased calcium release from the bone in patients with hyperthyroidism, increased release of calcitonin as a result of thyroid hormone manipulation in the thyroid gland, development of hypoalbuminemia and blood loss causing haemodilution with increased renal excretion of calcium, and autoimmune-related fibrosis of the blood vessels to parathyroid glands.

The demographical risk factors also contribute to postoperative hypocalcaemia following total thyroidectomy such as age (higher incidence among younger age), gender (women being more prone to calcium and vitamin D deficiency than men). Pathologically, the patients may have thyroiditis and thyroid carcinoma. Thyroid gland size, substernal extension of the thyroid, type of thyroid disorder, extent of surgery, and whether re-operation is necessary are other important risk factors.

In several series, the incidence of postoperative hypocalcaemia after total thyroidectomy varied from 1.6% to 50% but may be as high as 83%.¹⁰

Some group of researchers tried to define hypocalcaemia biochemically whereas some others tried to define clinically. Biochemical hypocalcaemia has been defined on the basis of serum thresholds where serum calcium concentration is less than 2 mmol/l (normal range 2.12 mmol/l-2.6 mmol/l). Clinically it has been defined as experiencing signs or symptoms of hypocalcaemia like numbness or paraesthesia of the face, fingers or toes, or positive Chvostek's (Tapping over the facial nerve will cause contraction of the facial muscles, it appears early) or Trousseau's signs (carpopedal spasm provoked by occlusion of the circulation to the arm), tetany and/or having serum calcium level lower than 2 mmol/l.¹¹

The symptoms of clinical hypocalcaemia are often distressing when severe and the prognosis is poor. The early post-operative clinical manifestations also carry poor prognosis. The condition presents dramatically 2-5 days postoperatively and the delay of the appearance of hypocalcaemia to 2-3 weeks is very rare.

The first clinical presentation of hypocalcaemia patient, such as circumoral tingling, paraesthesia or numbness, tingling of the fingers and toes, distal extremity muscle cramps and intense anxiety occur soon after surgery. Bronchospasm, laryngeal spasm (causing breathing difficulties), seizures (convulsions), or cardiac

arrhythmias may occur in more severe cases. Other symptoms of the condition include high levels of phosphate in the blood and low levels of parathyroid hormone, which can lead to abdominal, leg, and facial pain. After the surgery, a lack of parathyroid hormone can cause hypocalcemia, which may become apparent within one week and should be suspected if the patient appears overly agitated, depressed, or hyperventilates. In cases of chronic hypocalcemia and high phosphate levels, patients may experience dry hair, scaly skin, brittle nails, weakened tooth enamel, cataracts, and painful menstruation.

Hypocalcemia following thyroid surgery is often self-limiting, but it can also have potentially dangerous consequences. Although long-lasting effects are rare in transient hypocalcemia, patients experiencing immediate post-operative symptoms may require extended hospitalization and additional biochemical tests, significantly increasing the overall cost of thyroidectomy. Long-term morbidity due to permanent hypocalcemia following thyroidectomy places a considerable medical burden on patients, requiring prolonged treatment.

The objective of this observational study is to determine the frequency of hypocalcaemia following total and completion thyroidectomy.

METHODS

Study design

It was cross sectional observational study.

Place of study

Study conducted at department of otolaryngology and head neck surgery, Kurmitola general hospital and armed forces medical college, Dhaka.

Period of study

Study carried out from January 2020 to December 2020.

Study population

Patients undergoing total and completion thyroidectomy in dept. of otolaryngology and head-neck surgery, Kurmitola general hospital and armed forces medical college, Dhaka attending in prescribed follow up schedule during 12 months of study duration selected.

Sampling method

During the six-month study at the department of otolaryngology and head-neck surgery at Kurmitola general hospital and armed forces medical college in Dhaka, all patients who underwent total and completion thyroidectomy and attended the prescribed follow-up schedule were included using convenience sampling. The

structured questionnaire data sheet recorded patient particulars (name, age, sex, blood group), medical records, clinical examination findings, indication of thyroidectomy, operation notes, postoperative follow-up, and investigations. Specifically, the clinical presentation and serum calcium level of patients on specific postoperative follow-up days were also recorded.

Sample size

Samples were collected over a 12-month study period to ensure sufficient number for robust statistical analysis.

Sample size was determined by the formula: $(n) = Z^2 pq / d^2$

p= Expected proportion of event, (25% mean of 1.6-50% Abboud et al) it is regarded as 0.25 (25%).¹²

$q = 1 - p = 0.75$

Z=z-value of standard normal distribution at a given level of significance or, at a given confidence level (0.5 at 5% level of significance or 95% confidence level. Z=1.96), d(e)=Acceptable error. It is usually set at 5% (0.05).

So, sample size $n = (1.96)^2 \times 0.25 \times 0.75 / (0.05)^2 = 288.12$.

According to this formula the targeted sample is 288.12.

Since the study period was 12 months and COVID-19 pandemic situation of country, the number of samples could not be handled in this short period of time.

Therefore, the sample size was reduced to 30.

Inclusion criteria

All the patients undergoing total thyroidectomy and all the patients undergoing completion thyroidectomy were included in study.

Exclusion criteria

Lobectomy, hemithyroidectomy and dropout cases from follow up were excluded.

Operational definition

Hypocalcaemia: A decrease in the calcium level in plasma below 8mg/dl is termed hypocalcaemia.

Thyroid surgery: Total, or completion thyroid surgery.

Extensive thyroidectomy: Total thyroidectomy with selective neck dissection.

Transient (Temporary) hypocalcaemia: Calcium supplementation is required less than 6 months after surgery.

Permanent hypocalcaemia: Calcium supplementation is required more than 6 months after surgery.

Main outcome variables studied: Hypocalcaemia after thyroid surgery.

Confounding variable: Indication of surgery and varieties of disease.

Procedures of preparing and organizing materials: A questionnaire and a consent form prepared, samples were selected on the basis of inclusion and exclusion criteria, questionnaires were filled with informed written consent.

Materials used: computer laptop, printer, scanner, internet modem, data sheet.

Procedures of collecting data

Informed consent was taken from the patient or legal guardian of the patient. They were explained and counselled about the study.

Serum calcium level was noted before surgery, 24 hours, 48 hours and 72 hours after surgery, during sign symptom of tetany and during hospital discharge.

Patients were followed for any complication after surgery.

Data were collected as per designed data collection sheet by taking history, clinical examination, investigations and surgical treatment

A standard questionnaire has been formulated and patients were interviewed with questionnaire.

Professional assistance from experts

Professional assistance was taken from expert surgeons of the department of otolaryngology and head-neck surgery, Kurmitola general hospital and armed forces medical college, Dhaka.

Procedures of data analysis and interpretation

Tabulation, graphical presentation and analysis were done by SPSS-17

Quality assurance strategy

Caution was taken during data collection, caution was taken during data processing and data was analysed cautiously with SPSS-17.

Ethical implication

Prior to commencement of the study, the aims and objectives of the study along with its procedure, risk and

benefit were explained to the patients. It was assured that all information and records would be kept confidential and the procedure would be helpful for both attending surgeons and patients in making decision for management.

RESULTS

Among 30 patients 13 experienced hypocalcaemia at 24 hours, 48 hours and 72 hours after removal of specimen of surgery. The patients were selected according to the eligibility criteria. A preformed data collection sheet regarding patient profile, disease profile, surgical profile was filled up appropriately from the very beginning of the admission through the course of the treatment. The data regarding sex distribution, calcaemic status, calcium quantity, symptom status, diagnosis, type of operation as well as amount of calcium at different period mentioned above were collected. The data were edited, cleaned, decorated and analysed. The statistical significance was determined by unpaired t test. The level of significance was determined as <0.05 . The observations and results regarding the study are depicted in tabular and figure from the next page.

Sex distribution of the study patients

Among 30 patients, 9 (30%) were male and 21 (70%) were female patients. So, male to female ratio was 1:2.3.

Table 1: Sex distribution of the study patients, (n=30).

Sex	N	Percentage (%)	Ratio (Male: Female)
Male	9	30	1: 2.3
Female	21	70	
Total	30	100	

Distribution of surgical indication in different diseases

Different indications of thyroid surgery of the patients who underwent total thyroidectomy and completion thyroidectomy are displayed below. Among them the highest number of indications belong to papillary thyroid malignancy (43.33%) followed by multinodular goitre (36.67%).

Table 2: Distribution of surgical indication in different diseases, (n=30).

Name of diseases	N	Percentage (%)
Papillary carcinoma	13	43.33
Multinodular goitre	11	36.67
Follicular carcinoma	04	13.33
Hashimoto's thyroiditis	02	06.67
Total	30	100

Distribution of postoperative calcium status in blood

Out of 30 patients under went different thyroid surgery total 13 patients experienced hypocalcaemia among which 9 (69.23%) female and 4 (30.77%) were male.

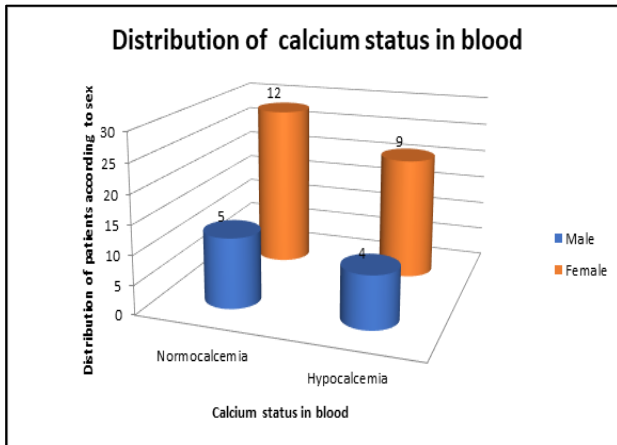


Figure 1: Distribution of postoperative hypocalcaemia and normocalcaemic patients, (n=30).

Distribution of symptoms of hypocalcaemia

Out of 13 patients of postoperative hypocalcaemia only 3 patients manifested symptoms in favour of hypocalcaemia.

Table 3: Distribution of symptomatic hypocalcaemic and asymptomatic hypocalcaemic patients, (n=13).

Presence or absence of symptoms	N	Percentage (%)
Asymptomatic (subclinal) hypocalcaemia	10	76.92
Symptomatic hypocalcaemia	03	23.08
Total	13	100

Distribution of postoperative hypocalcaemia developing time

Among 13 patients, maximum number (05) developed hypocalcemia after 24 hours of surgery and no patient developed hypocalcemia at 5th and 7th postoperative day.

Table 4: Distribution of postoperative hypocalcaemia developing time, (n=13).

Developing time of hypocalcaemia	N	Percentage (%)
After 24 hours of surgery	05	46.15
After 48 hours of surgery	06	38.46
After 72 hours of surgery	02	15.39
At 5 th postoperative day	00	00
At 7 th postoperative day	00	00
Total	13	100

Distribution of hypocalcaemia in different diseases

The different indications of thyroid surgery of the patients who developed postoperative hypocalcaemia are displayed below. Among them the highest number of hypocalcemia belong to papillary thyroid malignancy (46.15%) followed by multinodular goiter (30.77%). Hashimoto's thyroiditis belongs to the lowest number of indications of thyroid surgery (7.69%).

Table 5: Distribution of hypocalcaemia in different diseases, (n=13).

Indications of thyroid surgery	N	Percentage (%)
Papillary carcinoma	06	46.15
Multi nodular goitre	04	30.77
Follicular carcinoma	02	15.39
Hashimoto's thyroiditis	01	7.69
Total	13	100

Distribution of postoperative serum calcium status depending on type of thyroid surgery

The highest number of patients manifested postoperative hypocalcaemia after total thyroidectomy. They were 11 in number out of 24.

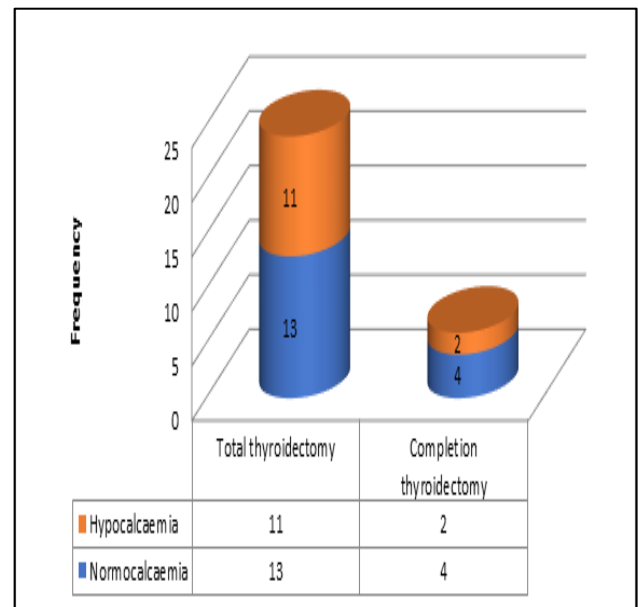


Figure 2: Distribution of postoperative serum calcium status depending on type of thyroid surgery, (n=30).

Distribution of with or without cervical lymph node dissection and percentage of hypocalcaemia

Among the 30 patients, 10 underwent thyroid surgery with cervical lymph node dissection, while 20 underwent surgery without lymph node dissection. Out of the 10 patients who had cervical lymph node dissections, 6 developed hypocalcemia (60%).

Table 6: Distribution of with or without cervical lymph node dissection and percentage of hypocalcaemia, (n=30).

Surgery	N	No. of hypo-calcaemia	Percentage of hypo-calcaemia (%)
With neck dissection	10	06	60
Without neck dissection	20	07	35
Total	30	13	

Pre-and postoperative serum calcium (Ca++) level of the study subjects at different time intervals

The serum calcium levels were observed preoperatively and at various time points after the surgery.

Table 7: Serum calcium (Ca++) level (mmol/L) in all patients, (n=30).

Serum calcium level	Mean±SD (mmol/L)	Min- Max (mmol/L)
Preoperative	2.2±0.2	2.0-2.6
After 24 hours (of surgery)	2.0±0.2	1.6-2.5
After 48 hours (of surgery)	2.0±0.3	1.5-2.5
After 72hours (of surgery)	2.0±0.2	1.5-2.6
At 5 th postoperative day	2.2±0.2	2.0-2.5
At 7 th postoperative day	2.3±0.3	2.0-2.6

Distribution of serum calcium status between normocalcaemia and hypocalcaemia patients at different times

Out of 30 patients, the serum calcium levels of both normocalcaemia and hypocalcaemia patients at different time intervals after the operation are compared below.

Table 8: Comparison of after 24 hours, after 48 hours and after 72 hours calcium (Ca++) level between hypocalcaemia and normocalcaemia patients, (n=30).

Serum calcium level, (mmol/l)	Hypo-calcaemia pt. (mmol/l), mean ±SD	Normo-calcaemia pt. (mmol/l), mean ±SD	P value
After 24 hours	1.9±0.2	2.1±0.1	0.001 ^s
After 48 hours	1.8±0.2	2.2±0.2	0.001 ^s
After 72 hours	1.8±0.1	2.1±0.1	0.001 ^s

*S=Significant, P value reached from unpaired t-test.

DISCUSSION

In our study, we concentrated on clinically significant hypocalcemia and identified hypocalcemic patients as those with a serum calcium level below 2.0 mmol/L.¹³ Postoperative hypocalcemia following thyroid surgery has been reported to occur in 1.6% to 50% of cases.¹² The majority of these cases involved transient hypocalcemia, which resolved into normal calcium levels within a few months with the help of calcium supplementation.

Approaches to prediction of hypocalcaemia are based on serum calcium values at different times after surgery have proven useful.¹⁴ The purpose of this study was to evaluate the ability of consecutive serum calcium level measurements in predicting hypocalcaemia at the time after thyroid surgeries.

In this study, a total 30 cases were evaluated. The mean age of the patients was 40.15±13.18 years ranging from 18 to 75 years. In study by Qari FA reported that mean age (mean±SD) was 39.35±13.97 which is consistent with this study.¹⁵

Thyroid diseases are more common in females.¹⁶ In this study, 9 were male and 21 were female. The male-female ratio was 1:2.3. So, our observation is consistent with the others.

Hypocalcaemia is more common in female after total thyroidectomy. In our study, hypocalcaemic patients were 13, of which 30.77% were male and 69.23% were female. Females are more prone to develop hypocalcaemia. In a comprehensive review by Eismontas et al the female gender is an independent risk factor for development of hypocalcaemia.¹⁷ So, this observation is also consistent with that of others.

During thyroidectomy and exploration of the thyroid lobes, parathyroid may be injured leading to devascularization or accidentally removed. Surgeon's basic knowledge regarding anatomy of parathyroids as well as technical expertise has major impact in preventing this sort of injury. Avoiding injury or proper per operative recognition of injury may be managed by auto transplantation of parathyroid in sternocleidomastoid, brachioradialis muscles. This type of management markedly reduces the incidence of permanent hypocalcaemia.¹⁸

To prevent permanent hypocalcemia, it is important to keep the dissection plane near the thyroid gland capsule and to close off the branches of the inferior thyroid artery close to the thyroid capsule.¹⁹ The risk of permanent hypoparathyroidism after thyroidectomy ranges from 0 to 10%. In our study, none of the patients were found to have permanent hypocalcemia, likely due to the short study period and the impact of the COVID-19 pandemic.

Patients were stratified into the 'hypocalcaemic' and 'normocalcaemic' groups depending on whether they had a postoperative calcium level less than 2.00 mmol/L. Out of 30 patients, 17 were normocalcaemic, and 13 were hypocalcaemic. Mean $\pm$ SD of the calcium levels after 24 hours, 48 hours, and 72 hours was 2.1 $\pm$ 0.1, 2.2 $\pm$ 0.2, and 2.1 $\pm$ 0.1 mmol/L, respectively.

In this study, postoperative hypocalcemia was identified more frequently in primary total thyroidectomies than in second surgical procedures (completion thyroidectomies). Most cases of postoperative hypocalcemia are able to recover. Completing a total thyroidectomy in a second surgical procedure enables the recovery of parathyroid glands that may have been affected during the first intervention. In the study by Prim et al postoperative hypocalcemia was also identified more frequently among primary total thyroidectomies than among those performed in a second surgical procedure to complete total thyroidectomy in patients previously diagnosed with carcinoma following a hemithyroidectomy for benign disease.²⁰ So, this study's findings are consistent with others. The frequency of hypocalcemia in our study was 45.83% after total thyroidectomy. Post-operative hypocalcemia after total thyroidectomy has been reported to range from 1.6% to 50%.¹² Therefore, the incidence of hypocalcemia in this study falls within the norm found in other studies.

In our study, we observed hypocalcemia in a total of 13 patients. Among them, 76.92% had subclinical hypocalcemia, while 23.08% experienced symptomatic hypocalcemia. Interestingly, these findings closely mirror those reported by Eismontas et al where 23.3% of participants exhibited symptomatic hypocalcemia in a study involving 400 individuals.²¹

Diseases of thyroid gland is a contributing factor of developing post-thyroidectomy hypocalcaemia. Cancer, Hashimoto's thyroiditis, and Grave's disease are high risk disease processes that cause more post-thyroidectomy hypocalcaemia. In malignant diseases, hypocalcaemia may develop due to the vascular damage or the inadvertent parathyroidectomy due to invasion of thyroid capsule. In this study, hypocalcaemia developed in 46.15% papillary carcinoma patients, 30.77% in multinodular goitre patients, 15.39% in follicular carcinoma patients and 7.69% in Hashimoto's thyroiditis patients. In our study, we observed a higher incidence of hypocalcemia in patients with malignant goitre (25%) and toxic goitre (11.4%) compared to those with simple nodular goitre (3.6%) Sousa et al showed that incidence of postoperative hypocalcaemia is more in papillary carcinoma compared to follicular.^{22,23} Here, malignancy is also the first contributing factor of developing hypocalcaemia. So, it is consistent with the other study.

The risk of hypocalcemia is higher in patients who underwent thyroidectomy along with cervical lymph node dissection. In a study of 30 patients, 10 underwent

cervical lymph node dissection along with total and completion thyroidectomy, while 20 did not undergo cervical lymph node dissection along with total and completion thyroidectomy. Among the 10 patients who underwent cervical lymph node dissection, 6 (60%) developed hypocalcemia, while among the 20 patients who did not undergo cervical lymph node dissection, 7 (35%) developed hypocalcemia. According to a study by Azmi et al the risk of hypocalcemia was several times higher in patients who underwent cervical lymph node dissection compared to those who did not undergo this procedure during thyroid surgeries.²⁴ Therefore, our findings are consistent with this previous study.

Patients may experience hypocalcemia after thyroid surgery, typically within 24 to 48 hours post-surgery. However, in some cases, hypocalcemia may occur later.²⁵ Out of 13 patients who developed hypocalcemia, 6 experienced it after 24 hours, 5 after 48 hours, and 2 after 72 hours. The mean calcium levels after 24, 48, and 72 hours were significantly different ($p < 0.05$) between patients with hypocalcemia and those with normal calcium levels based on unpaired t test. This indicates that the timing of hypocalcemia development is consistent among patients.

After surgery, hypocalcemia may develop slowly over time. The symptoms of hypocalcemia can put the patient in difficult situations. In these cases, patients have to stay in the hospital for observation of their serum calcium levels after the symptoms occur and also take medications for recovery. However, only 3 patients in our study developed symptoms of hypocalcemia.

Limitations

Duration is short, sample size is small, Does not proclaim the scenario of whole country? study at COVID-19 pandemic period were limitations of the study.

CONCLUSION

The study indicates that the level of serum calcium significantly decreases after total thyroidectomy, especially within the first 72 hours after the procedure. Hypocalcemia occurred more frequently in females and in cases of malignant thyroid diseases. If there are no clinical signs or symptoms of hypocalcemia during this period, the patient is considered to be safe. These findings can help determine which patients can be discharged early and which ones may require close monitoring of calcium levels and early calcium supplementation.

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