ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 2, Issue – 6, November - December - 2019, Page No. : 97 - 106

Incidence of Hypocalcaemia in Total Thyroidectomy- A Prospective Study.

[1]Dr Anil Kumar M, Post Graduate, ESIC-MC PGIMSR Rajajinagar, Banagalore-560010.

[2]Dr Preetham Raj G, Assistant Professor, Department of General surgery, ESIC-MC PGIMSR, Rajajinagar, Banagalore-560010

Corresponding Author: Dr Preetham Raj G, Assistant Professor, Department of General surgery, ESIC-MC PGIMSR, Rajajinagar, Banagalore- 560010

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background & Objectives: Thyroidectomy performed for any cause leads to hypocalcaemia. Symptoms related to hypocalcaemia are observed usually 24 to 48 hours after the operation. There are patients and clinical conditions under risk for hypocalcaemia. Hence, Objective of the study to find the incidence of hypocalcemia following total thyroidectomy and occurrence of transient/temorary and permanent hypocalcaemia among total thyroidectomy patients.

Methods: A total of 50 total **t**thyroidectomy patients were enrolled in the study. Demographic, clinical profile, indication of surgery, biochemical and laboratory tests parameter were obtained. Pre-operative Serum calcium and ionized calcium were measured and post op checked for clinical signs and symptoms of Hypocalcemia including serial estimation of serum and ionized calcium. Post operatively hypocalcemic patients were followed up for duration of 6months. Data was analysed using SPSS.

Results: About 36% i.e 18 numbers of patients had post operatively hypocalcaemia. In that incidence of hypocalcemia among females, malignancy was higher. Total 17 subjects had transients' hypocalcaemia and 01 permanent hypocalcaemia.

Interpretation & Conclusion: The factors associated with hypocalcaemia were defined to be gender, preoperative diagnosis, parathyroid gland injury, etc hence it is a multifactorial problem and it would not be proper to define a few etiological factors.

Keywords: Hypocalcaemia, total thyroidectomy, Malignancy.

Introduction

Thyroid surgeries and radioiodine therapy are among the most common in the world.[1] Thyroid surgery is the definitive management option for thyroid malignancies, and also for benign diseases such as multinodular goiter with compression symptoms.[2] Thyroidectomy is frequently recommended to patients with thyroid nodules, especially for those in whom thyroid cancer is suspected of carrying thyroid cancer. The completeness of surgical resection helps to improve survival and lower recurrence; thus, most surgeons proposed total thyroidectomy over thyroid lobectomy. However, compared with thyroid lobectomy, there is a higher incidence risk of complications after total thyroidectomy.[3]

Complications of these surgical procedures are numerous, and some of them are severe and persistent over time, including hypoparathyroidism, hypocalcemia, vocal paralysis, and hemorrhage. Hypocalcemia following total

thyroidectomy (TT) is a relatively frequent complication, which is sometimes difficult to correct. Temporary hypocalcemia occurs in 50–68% of post-TT patients, while permanent hypocalcemia occurs in 3% of post-TT patients.[4]

Post-TT hypocalcemia depends on a number of factors, including biochemical blood parameters before and after surgery, clinical effects and factors related to surgery, surgical technique, surgeon's experience, the patient, and the disease.[1,4]

The British Association of Endocrine and Thyroid Surgeons (BAETS) registry defines post-thyroidectomy hypocalcaemia as corrected calcium less than 2.10mmol/l on first post-operative day (POD1) and the fourth national audit reported a rate of 24.9%. The reported incidence of post-thyroidectomy hypocalcaemia ranges from 3.1–100%. Permanent hypocalcaemia (need of treatment to maintain normocalcaemia at six months) was found in 12.1% of patients.[4,5]

Decreased serum calcium, secondary to hypoparathyroidism, may present clinically with muscle cramps, perioral and peripheral paresthesias, carpopedal spasm or tetany, and/or confusion. Symptomatic patients often require extended hospitalizations following thyroid surgery, leading to increased healthcare costs. Hypocalcemia can be permanent, requiring lifelong oral supplementation or transient, which would resolve in few months, depending on the extent of the damage to the parathyroid gland.[5,6]

Injury to the parathyroid glands (PTG) is generally accepted as the most common cause of post-thyroidectomy hypocalcaemia. This may be due to PTG devascularisation, obstruction of venous drainage or inadvertent PTG excision.[5] The intact PTH has a half-life in minutes and can be reliably assayed.

It is degraded into several smaller proteins with variable half-lives and biologic activity. The delay in appearance of postoperative hypocalcemia is up to 48 hours depending on the levels of such biologically active peptides as well as the patient's vitamin D and electrolyte status and the presence or absence of "hungry" bone, among other factors.[7]

Some surgeons have been advocating the routine use of postoperative oral calcium and/or vitamin D supplementation, to shorten the hospital stays by minimizing the incidence of hypocalcemia . Such routine use is particularly common in the outpatient or short-stay setting, where there is limited time available to correct hypocalcemia once it is discovered. (6) Early pharmacologic support with calcium, magnesium and calcitriol can potentially keep high-risk patients eucalcemic and asymptomatic, thereby avoiding morbidity. This is because of the lag between the hypo secretion of PTH and the development of symptomatic hypocalcemia. As a fat-soluble vitamin, its pharmacokinetics are such that an increase in serum calcium may take 24-48 hours.[7,8]

On the contrary, few surgeons opine in sending patients home with prescriptions for elemental calcium supplementation to be filled if symptoms of hypocalcemia develop. More recently, with the aim of finding an earlier predictor for hypocalcemia, the short half-life of the parathyroid hormone has led to increased interest in postoperative intact parathyroid hormone (IPTH) as an early marker of hypocalcemia. However, the routine measurement of IPTH to assess the risk of postoperative hypocalcemia has yet to become accepted as standard practice. The variability in assays, timing of measurements, and cutoff levels makes comparisons between studies difficult.[9,10]

The early identification of patients at risk of hyperparathyroidism and hypocalcemia, post-thyroidectomy, would allow for an early introduction of calcitriol. Patients at low risk of hypocalcemia, post-thyroidectomy, can be spared the discomfort of excessive blood tests and can reliably be discharged without fear of symptomatic hypocalcemia.[11,12]

This present study was conducted on the patients undergoing total thyroidectomy, to know the occurrence hypocalcemia among total thyroidectomy patients and to know the incidence of temporary and permanent hypocalcemia in total thyroidectomy.

Methodology

A prospective study was carried out in ESIC MC PGIMSR BENGALURU from January 2018 to June 2019 on Occurrence of hypocalcemia in total thyroidectomy patients.

Study Design: Prospective Study.

Study Period: From January 2018 To June 2019.

Sample Size: A total of 50 cases.

The sample size for the present study has been calculated by considering the 24% occurrence of hypocalcemia after the total thyroidectomy from the past published literature.[13] The minimum sample size has been calculated as 50 cases with 0.07 as absolute marginal error at 5% level of significance assuming two tailed hypothesis. Following formula has been used to calculate the sample size:

$$n = \frac{Z^2_{\alpha/2} PQ}{D^2}$$

Where, Zα/2 =1.96, P=.24, Q=1-P and D=0.07

Method of Data Collection

All the patients undergoing total thyroidectomy cases were examined and clinical diagnosis was made. Blood was collected in a plain sampling bottle pre-operatively for serum calcium and ionized calcium levels. Another sample of blood was collected between 24 to 48 hours post-operatively and submitted to the same to lab. If Signs and symptoms of hypocalcemia presents early estimation of serum and ionized calcium done at regular intervals. After discharge patients were followed up for 1month and hypocalcemic patients for duration of 6months with estimation of serum and ionized calcium done after stopping calcium supplementation 1 day prior. Hypocalcemia for the study was defined as serum calcium level below 8 mgs/dl and ionized calcium below 4.4mg/dl. Transient hypocalcemia was defined as serum calcium level below 8 mgs/dl for a period of less than 6months and permanent hypocalcemia for more than 6 months.

All the patients included in this study were subjected to biochemical and laboratory tests like routine hematological investigations, blood sugar, serum electrolytes, renal function test, liver function tests. Additional tests like the Thyroid function test was conducted which included serum TSH, serum free T3 and T4.

Imaging was included as one of the tests for the subjects to be included into the study. Radiological examination performed were chest X-ray including soft tissue of neck and ultrasound of neck, FNAC and indirect laryngoscopy.

Management of hypocalcemia will be done by using oral or intravenous calcium supplementation with or without vit D and assessing the outcome of medical management of hypocalcemia.

Inclusion Criteria

1. Patients who give written informed consent after reviewing the informed consent document.
2. Patients undergoing total thyroidectomy above 12 years.

Exclusion Criteria

1. Patients with co morbid conditions like Medical renal disease, chronic liver disease.
2. Patients on calcium medications.
3. Patients on vitamin D medications.
4. Patients not willing for the study.

Statistical Analyses

The data collected were entered into excel spread sheet and it was analyzed using the Statistical Package for Social Sciences (SPSS) version 22.Descriptive and inferential statistics was done. Chi square test for proportion and independent t test for comparison of means was used. Statistical significance was considered at p <0.05 (confidence interval of 95% was taken).

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

Chi-square ($\chi 2$)

The subscript "c" is the degrees of freedom. "O" is observed value and E is expected value.

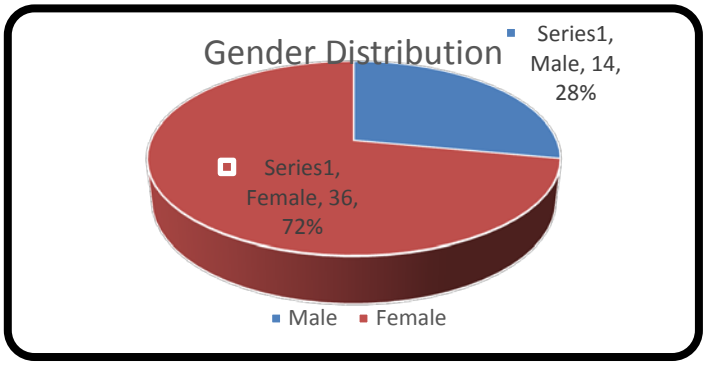
Training and Calibration

Principal investigator was trained and calibrated in the Department of Surgery, ESICMR PGIMSR Hospital, Bengaluru prior to start of the study to ensure reliability. The overall intra-examiner reliability was good and these values reflected high degree of conformity in observation.

Results

Table 1: Gender Distribution of the Study Population

Gender	Total Number
Male	14
Female	36
Total	50

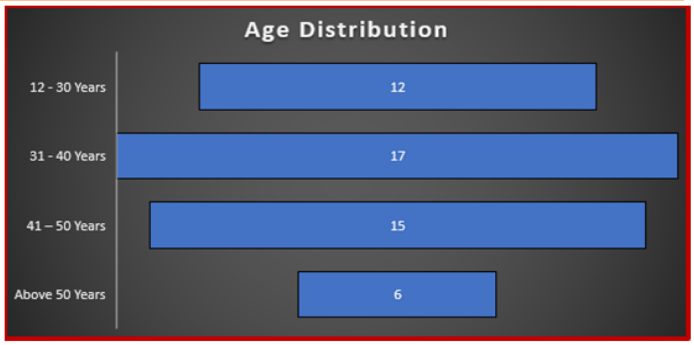


In This Study We Followed 36 Female Patients And 14 Male Patients Who Underwent Total Thyroidectomy

Age Distribution of Study Population

Table 2: Age Distribution of the Study Population

Age Distribution	Total Number
12 - 30 Years	12
31 - 40 Years	17
41 – 50 Years	15
Above 50 Years	06



1)12 people fall in Age group of 12-30years

2)17 people fall in Age group of 31-40 years

3)15 people fall in Age group of 41-50years

4)6 people fall in Age group of above 50years

Table 3: Pre Operative Indications for Total Thyroidectomy in Study Population

Pre-operative indications for Total Thyroidectomy	Total number
Malignancy	05
Toxic Features	12
Swelling/Goitre	33
Total	50

According to the preoperative indications of thyroidectomy, out of 50 patients, 05 patients were posted for thyroidectomy for suspecting malignancy, 12 patients were posted for thyroidectomy for toxic features after controlling toxicity, and 33 patients were posted for thyroidectomy for complaints like swelling or goitre or pressure effects.

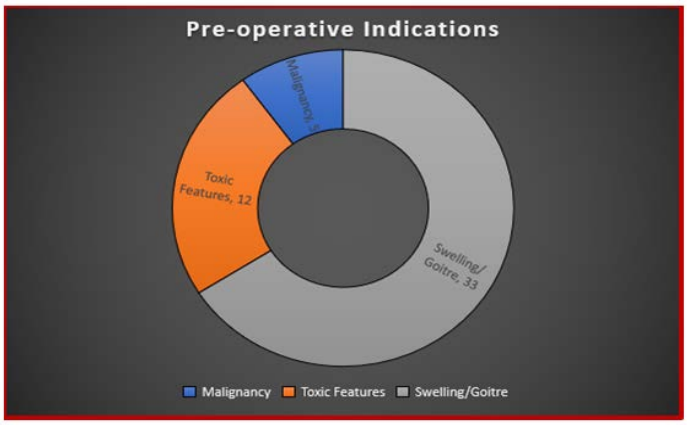
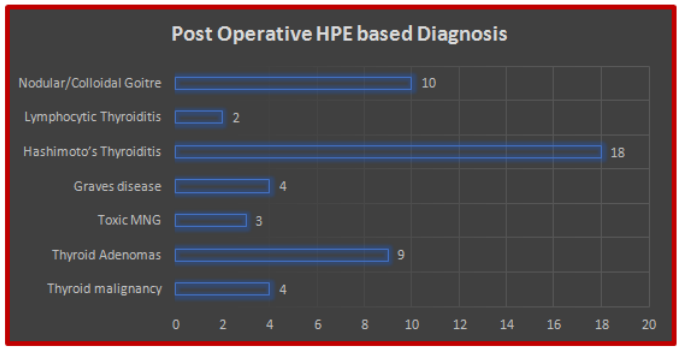


Table 4: Post Operative Hpe Based Diagnosis of Study Population

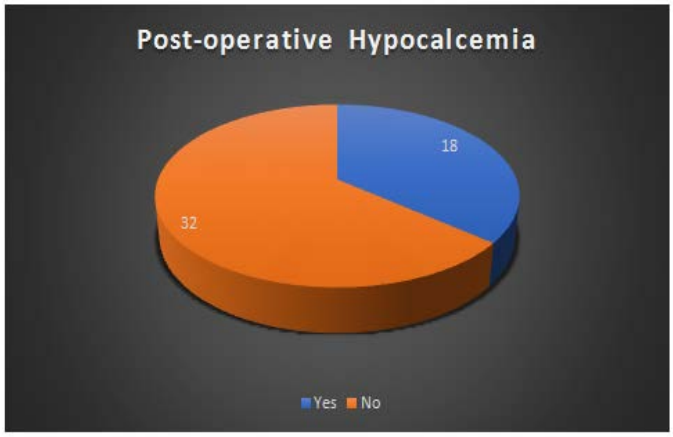
Diagnosis	Number of cases studied
Thyroid malignancy	04
Thyroid Adenomas	09
Toxic MNG	03
Graves disease	04
Hashimoto's Thyroiditis	18
Lymphocytic Thyroiditis	02
Nodular/Colloidal Goitre	10
Total cases	50



Out of the 50 total thyroidectomised patients, postoperative follow up shows the following HPE reports. Four patients underwent total thyroidectomy shows Papillary thyroid carcinoma in their specimen, 09 patients showing thyroid adenoma, 03 patients HPE report reveals toxic multinodular goitre and 04 patients specimen shows Graves disease. Hashimotos thyroiditis reported in post thyroidectomy specimens of 18 patients and lymphocytic thyroiditis in 02 patient and 10 patients with nodular or colloid goitre

Table 5: Incidence of Post Thyroidectomy Hypocalcaemia In Study Population

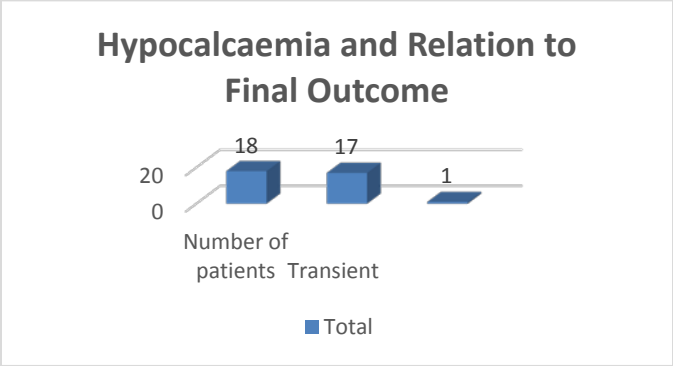
Post-operative Hypocalcemia	Total Number (%)
Yes	18 (36%)
No	32 (64%)



In our study period we documented 18 patients out of 50 patients of study population had experienced signs and symptoms of hypocalcemia in their post- operative period It denotes approximately 36% of study population experienced hypocalcemia in their post- operative period.

Table 6 : Incidence Of Post Thyroidectomy Temporary And Permanent Hypocalcaemia In Study Population

Hypocalcemia	Number
Temporary	17
Permanent	1



Out of 18 Hypocalcemic patients 17 had Temporary and 1 had Permanent Hypocalcemia.

Table 7: Gender Based Incidence Of Post Thyroidectomy Hypocalcaemia

Gender	Number of patients	Post Thyroidectomy Hypocalcemia
Male	14	7
Female	36	11

07 out of 14 male patients experienced hypocalcaemia in their post-operative period, approximating to 14%.

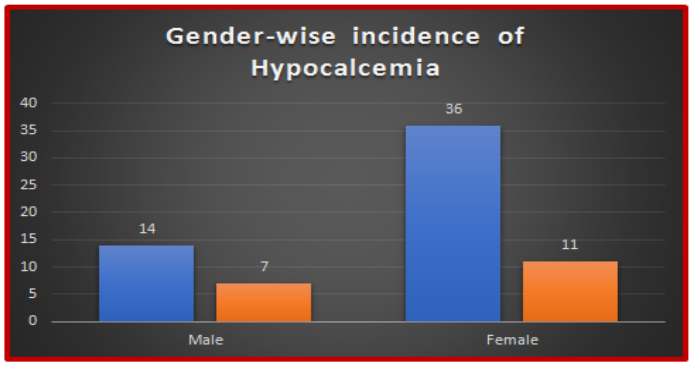
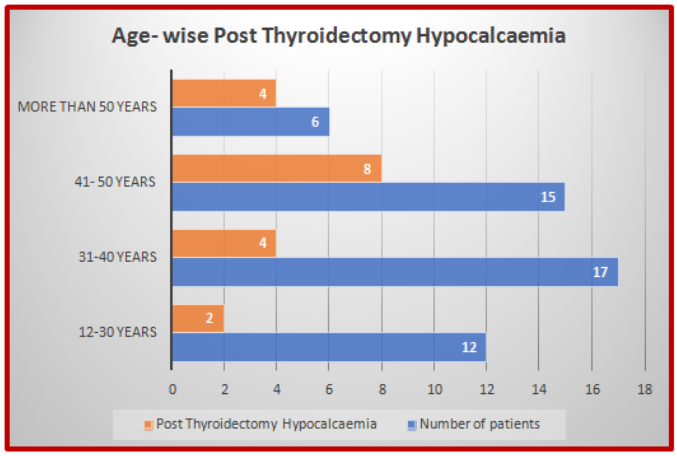


Table 8: Incidence of Post Thyroidectomy Hypocalcaemia in Relation to Age In Study Population

Age Distribution Of Study Population	Number Of Patients	Post Thyroidectomy Hypocalcemia
12-30 Years	12	02
31-40 Years	17	04
41- 50 Years	15	08
More Than 50 Years	06	04



According to age distribution 2 patients in the age group of 12 to 30 years and 4 patients in the age group of 31 to 40 years, and 8 patients in the age group of 41 to 50 years and 4 patients in the age group of more than 50 years are affected by post-operative hypocalcemia.

Approximately, 16 % of 12 to 30 years patients experienced post-operative hypocalcemia, 23% of 31 to 40 years experienced hypocalcemia, and 53 % of 41 to 50 years experienced hypocalcemia and 66% of more than 50 years experienced post-operative hypocalcemia

Table 9: Incidence of Post Thyroidectomy Hypocalcaemia In Relation To Pre Op Indications In Study Population

Pre-operative indications for Thyroidectomy	Number of Patients	Post-Thyroidectomy Hypocalcemia	Percentage
Malignancy	04	04	100%
Toxic Features	12	08	66%
Swelling/Goitre	24	06	25%

Patients who underwent total thyroidectomy with pre-operative diagnosis of malignancy experienced 100 % of postoperative hypocalcaemia and approximately 66% of patients with toxic features experienced postoperative

hypocalcemia. Only 25% of patients with swelling or goitre are reported with postoperative hypocalcaemia.

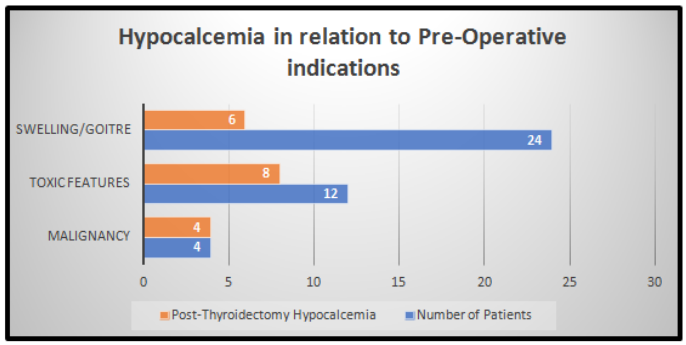
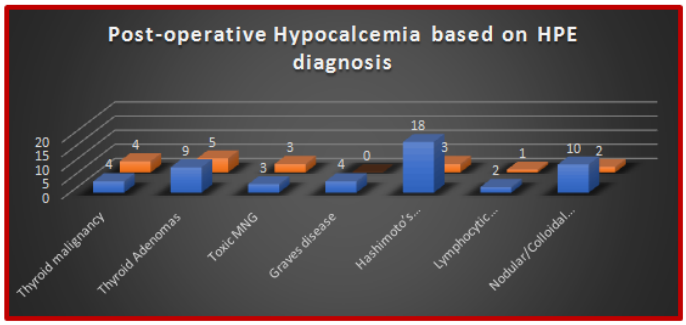


Table 10: Incidence of Post Thyroidectomy Hypocalcaemia in relation to Post Operative HPE

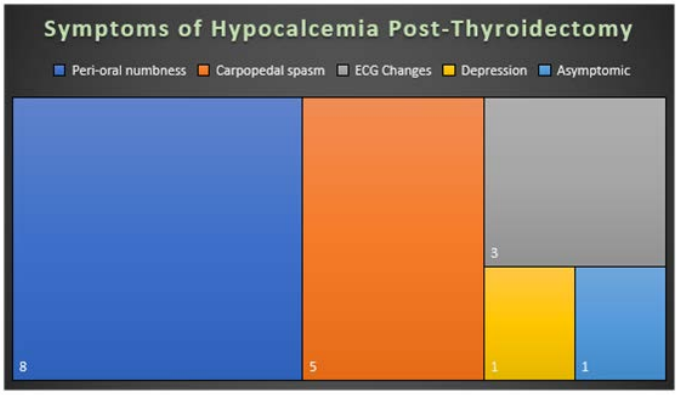
Diagnosis	Number of cases studied	Post Thyroidectomy Hypocalcemia
Thyroid malignancy	04	04
Thyroid Adenomas	09	05
Toxic MNG	03	03
Graves disease	04	00
Hashimoto's Thyroiditis	18	03
Lymphocytic Thyroiditis	02	01
Nodular/Colloidal Goitre	10	02
Total cases	50	18



According to final postoperative HPE based diagnosis, the incidence of post thyroidectomy hypocalcaemia experience in our study was 4 out of 4 thyroid malignant patients experienced post thyroidectomy hypocalcaemia and 55 % of thyroid adenomas, and 100% of toxic multinodular goitre patients and 50% of Hashimotos thyroiditis patients and 20% of nodular or colloid goitre patients experienced post operative hypocalcaemia.

Table 11: Presenting Feature of Post Thyroidectomy Hypocalcaemia In Study Population

Presenting symptoms of Post-Thyroidectomy Hypocalcemia	Number of Patients
Peri-oral numbness	8
Carpopedal spasm	5
ECG Changes	3
Depression	1
Asymptomic	1



Out of 18 patients experiencing Hypocalcemia post Thyroidectomy, 8 patients presented symptoms of Peri-oral numbness, 5 patients with carpopedal spasm, 3 with ECG changes, 1 with depression and 1 was asymptomic .

Discussion

The present study aimed at identifying the patients at high risk of developing hypocalcaemia and occurrence of transient/temporary and permanent hypocalcemia following total thyroidectomy. Hypocalcaemia is defined as serum calcium less than 8mg/dl. Mildly low levels that develop slowly often have no symptoms. Otherwise symptoms may include numbness, muscle spasms, seizures, confusion, or cardiac arrest.

Unal et al found that the rates of transient and permanent hypocalcaemia were significantly high in women. In the present study, gender was found to be a significant risk factor in hypocalcaemia. Our study population also

reflects the same. The study population included 28% males and females contributed to 72% of the total study population. In our study, results show that thyroid diseases that may need thyroid surgeries are frequent in the middle age group between 31 and 40 years. However, the post-thyroidectomy hypocalcemia incidence is more common among females and in the advancing age group, i.e., more than 40 years. This may be probably since there were more females presenting with thyroid symptoms in our study and the majority of patients were above 40 years of age.[5]

In our study the incidence of hypocalcemia in total thyroidectomy for malignancy was 100% and similar results were obtained in the study "Clinical study of hypocalcemia following thyroid surgery by Senthil Arumugam et al."[14]

In our study the incidence of permanent hypocalcemia was 2% and similar results were obtained in the study of Pattou F, Combemale F, Fabre S, Carnaille B, Decoulx M, Wemeau JL et al. i.e incidence of permanent hypocalcemia ranged from 1 to 3%.

Therefore the results obtained from our study could be comparable with other studies With all these inputs we will be able to manage thyroid surgeries more efficiently and thus bringing down the morbidity and mortality among patients.

Conclusion

Post-thyroidectomy transient hypocalcemia is the most common complication which can be prevented with pre-operative preparation of patients with extreme caution and intra-operative meticulous dissection, prompt identification of parathyroid and post-operative frequent monitoring of serum calcium and early treatment can prevent significant morbidity.

In the present study, the overall incidence of developing post-thyroidectomy hypocalcemia is 36%. In that 34% was transient/temporary and only 2% were permanent hypocalcemic who were on calcium supplements. Also, it was noticed that the female patients were more likely to develop Hypocalcemia since thyroid disorders were common in them. Hence, it is recommended to have a calcium level evaluation pre and post operation also to look for signs and symptoms of hypocalcemia in asymptomatic patients

Hence from our study it can be concluded that incidence of hypocalcemia is more in females, age group above 40years, diagnosed cases of thyroid malignancy and toxic MNG however prevention of hypocalcemia can be achieved with peo op normal calcium levels and intra op meticulous dissection of thyroid gland with identification of atleast two parathyroid glands and if incidental parathyroidectomy done auto transplantation to be considered.

Summary

In summary, postoperative hypocalcemia is a multifactorial, problematic source of morbidity among thyroid surgery patients, resulting in longer hospital stays and thereby increased procedure costs. Interventions such as routine oral calcium and/or vitamin D supplements have been shown to reduce the incidence of hypocalcemia and may be particularly beneficial in patients at risk, including those with malignancy and/or individuals undergoing total thyroidectomy. With the use of extensive and ambulatory thyroid surgery to treat benign conditions such as multinodular goiter, close monitoring of patients at risk for the development of hypocalcemia is particularly warranted.

The current study was conducted to assess hypocalcemia post total thyroidectomy. The major highlights of this study are as follows:

36 Females and 14 males participated in the study.

Maximum participants i.e 17 were from the middle age group (31- 40 years)

Maximum participants were admitted with the chief complaint as Swelling/Goitre (33).

Total Thyroidectomies were performed for 50 subjects.

HPE based diagnosis revealed maximum subjects had Hashimoto's thyroiditis (18) followed by Nodular/colloidal goiter (10).

36% of the subjects (18) were tested positive for Post-Thyroidectomy Hypocalcaemia, out of which, 11 were females and 7 males.

Out of 36% of the subjects 17 were categorized into transient/temporary and 1 as a permanent hypocalcemia after a follow up duration of 6months.

The 41-50 years age group formed the maximum portion of participants with hypocalcemia.

All participants with malignancies complained of post-operative hypocalcemia, followed by the subjects toxic features (66%).

Based on the HPE diagnosis, out of 18 subjects with Hashimoto's Thyroiditis, 3 showed symptoms of Hypocalcemia. 5 out of 9 Thyroid Adenoma subjects were present with hypocalcemia, while, all the subjects with malignancies had hypocalcemia.

Peri-oral numbness was the most common symptom of hypocalcemia observed (8), followed by Carpopedal spasm (5).

There is a strong need of future studies to further investigate newly identified and controversial predictors of postoperative hypocalcemia, including ethnicity and younger age, with the goal of ultimately reducing the incidence, cost, and long-term effects of this common complication.

References

1. Eismontas V, Slepavicius A, Janusonis V, Zeromskas P, Beisa V, Strupas K, Dambrauskas Z, Gulbinas A, Martinkenas A. Predictors of postoperative hypocalcemia occurring after a total thyroidectomy: results of prospective multicenter study. BMC surgery. 2018 Dec;18(1):55.
2. Jaan S, Sehgal A, Wani RA, Wani MA, Wani KA, Laway BA. Usefulness of pre-and post-operative calcium and Vitamin D supplementation in prevention of hypocalcemia after total thyroidectomy: A randomized controlled trial. Indian journal of endocrinology and metabolism. 2017 Jan;21(1):51.
3. Wang YH, Bhandari A, Yang F, Zhang W, Xue LJ, Liu HG, Zhang XH, Chen CZ. Risk factors for hypocalcemia and hypoparathyroidism following thyroidectomy: a retrospective Chinese population study. Cancer management and research. 2017;9:627.
4. Vargas-Pinto S, Arenas MA. Lobectomy compared to total thyroidectomy for low-risk papillary thyroid cancer: A systematic review. Journal of Surgical Research. 2019 Oct 1;242:244-51.
5. Edafe O, Prasad P, Harrison BJ, Balasubramanian SP. Incidence and predictors of post-thyroidectomy hypocalcaemia in a tertiary endocrine surgical unit. The Annals of The Royal College of Surgeons of England. 2014 Apr;96(3):219-23.
6. Baldassarre RL, Chang DC, Brumund KT, Bouvet M. Predictors of hypocalcemia after thyroidectomy: results from the nationwide inpatient sample. ISRN surgery. 2012 Jul 15;2012.
7. AlQahtani A, Parsyan A, Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. Canadian Journal of Surgery. 2014 Aug;57(4):237.
8. Schafer AL, Shoback DM. Hypocalcemia: Diagnosis and treatment. InEndotext [Internet] 2016 Jan 3. MDText. com, Inc..
9. Noureldine SI, Genther DJ, Lopez M, Agrawal N, Tufano RP. Early predictors of hypocalcemia after total thyroidectomy: an analysis of 304 patients using

a short-stay monitoring protocol. JAMA Otolaryngology–Head & Neck Surgery. 2014 Nov 1;140(11):1006-13.

10. Mazotas IG, Wang TS. The role and timing of parathyroid hormone determination after total thyroidectomy. Gland surgery. 2017 Dec;6(Suppl 1):S38.
11. AlQahtani A, Parsyan A, Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. Canadian Journal of Surgery. 2014 Aug;57(4):237.
12. Puzziello A, Gervasi R, Orlando G, Innaro N, Vitale M, Sacco R. Hypocalcaemia after total thyroidectomy: could intact parathyroid hormone be a predictive factor for transient postoperative hypocalcemia?. Surgery. 2015 Feb 1;157(2):344-8.
13. Nair CG, Babu MJ, Menon R, Jacob P. Hypocalcaemia following total thyroidectomy: An analysis of 806 patients. Indian J Endocr Metab 2013;17:298-303.
14. Arumugam S, Mohankumar A, Muthukumaraswamy A, Anandan H. Clinical Study of Hypocalcemia following Thyroid Surgery. Int J Sci Stud 2017;4(11):37-41.