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Original Research Article

Incidence of Hypocalcaemia and its Clinical presentations following Total Thyroidectomy

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Abstract:

Background: Hypocalcaemia following Thyroid surgeries is one of the commonest complications all over the world. The amount of ionized calcium (Ca2+), contributes to the physiological and biochemical processes at the cellular level, rather than the total calcium. Hypocalcaemia was defined as a serum calcium level of <2.00 mmol/L in Post-thyroidectomy patients. Management of Hypocalcaemia was variable and dictated by variations in practice rather than patient needs and had its effect on the length of hospital stay as well as symptoms and signs.

Aim and Objectives of the study: To assess the occurrence of hypocalcaemia following Total thyroidectomy. To study various clinical presentations of post total thyroidectomy hypocalcaemia, day of appearance of its symptoms or fall in serum (Ca+) levels, correlation of the symptoms with the serum calcium levels, correlation of post total thyroidectomy hypocalcaemia with other indications of total thyroidectomy and its prevalence in relation to the age and gender.

Materials: 83 patients undergoing Total Thyroidectomy were included in the study. Serum Calcium levels were estimated at 4 to 6 hours postoperatively and again on day 1 and on day 2 postoperatively. Serum calcium levels were estimated every 2 weeks and then at 6 weeks after stopping supplemental therapy. If the patient becomes symptomatic original regimen restarted.

Results: Among the 83 patients majority of the patients belonged to the age group intervals of 36 to 45 and 46 to 55 years; 58 (69.87%). There were 61 (73.49%) females and 22 (26.50%) male patients among the total 83 patients in the study. The male to female ratio was 2.77:7. Hypocalcaemia developed in 13 (15.66%) on the first post-operative day, 19 (22.89%) on the second post-operative day and 23 (27.71%) developed on the third post-operative day. It was found that earlier the development of Hypocalcaemia shorter was the Hospital stay. The Mean Hospital stay was statistically lower and significant in the patients without developing Hypocalcaemia than those developing Hypocalcaemia (p value was 0.001).

Conclusions: The incidence of post-operative Hypocalcaemia was high on the 3rd Postoperative Day. The clinical manifestations of Hypocalcaemia were predominantly Perioral numbness and Paraesthesia, affecting a considerable proportion of patients. The symptoms were more prevalent in the age groups of 36-45 and 46-55 years. A statistically significant decrease in serum calcium levels was observed post-operatively, directly correlating with the development of clinical symptoms. These findings emphasize the critical role of early identification and management of Hypocalcaemia to mitigate patient discomfort and potential complications. Further research is warranted to explore the underlying mechanisms contributing to post-operative Hypocalcaemia and to identify potential predictive factors. Regular serum calcium monitoring and early intervention in patients undergoing. Total Thyroidectomy helps in to prevent the development of symptomatic Hypocalcaemia and improve overall patient outcomes.

Keywords: Thyroidectomy, Hypocalcaemia, Carpo-pedal spasm, Multinodular Goitre and perioral numbness

Introduction

Among the various complications that can develop following Total Thyroidectomy such as transient or permanent cord paralysis or severe bleeding and Hypocalcaemia, the last mentioned one is more frequent. [1] Post-total Thyroidectomy Hypocalcaemia arises due to inadvertent or

selective removal of the parathyroid glands. [2] Sometimes devascularization and damage to the parathyroid glands could result in induction of a state of transient (or permanent) Hypo-parathyroidism. [3] Other mechanisms which contribute too development of Hypocalcaemia are vitamin D deficiency, a sudden increase in Calcitonin serum levels (because of handling of the Thyroid gland during surgery) or an "hungry bone syndrome" [4,5,6,7,8]. In addition post-operative alkalosis-induced Hypocalcaemia may result in from hyperventilation triggered by postoperative pain, and dilution Hypocalcaemia [9]. Surgeon must keep in mind the possibility of development of Hypocalcaemia in post-thyroidectomy patients, to follow a protocol to treat the crisis of Hypocalcaemia which is a very important task in post-operative management. [10] Hypocalcaemia when detected earlier is easy to manage and it would reduce the laboratory investigative burden and reduce the hospital stay for the patient also. [11] Whenever Hypocalcaemia is predicted, prophylactic administration of Calcium and vitamin D supplements could avoid the development of Hypocalcaemia symptoms, signs and premature discharge of patients. [12] Many studies are available highlighting the risk factors related to development of early Hypocalcaemia (EH) following Total Thyroidectomy surgery, with variable observations and outcomes. [13] As the available predictors of Hypocalcaemia are limited in terms of clinical and laboratory, Post-operative Hypo-parathyroidism is a clinical challenge for Thyroid surgeons. [5]

Materials and Methods

Study Design: Prospective observational study.

Study Area: Malabar Area, Calicut, Kerala.

Study Population: 83 Patients admitted in General Surgery Departments of a Tertiary Care Centre, with thyroid disorders who needed total thyroidectomy.

Study Period: 36 months: From February 2020 to January 2023

83 patients who underwent Total Thyroidectomy surgery in the General Surgery Department of KMCT Medical College, Mukkom, Manassery, Kerala. An Institute Ethics committee approval was obtained before commencing the study and the Ethics committee approved consent form and proforma were used to collect the data.

Inclusion Criteria: Patients of both genders aged above 15 years and below 65 years were included. Patients presenting with thyroid dysfunction that required total thyroidectomy were included.

Exclusion Criteria: Patients aged below 15 years were excluded. Patients presenting with thyroid dysfunction that needed other than total thyroidectomy like hemi total thyroidectomy/subtotal thyroidectomy/near total thyroidectomy were excluded. Patients with Poor calcium intake over a long period of time, especially in childhood– malnutrition were excluded. Patients with medication that decreased calcium absorption or caused mal absorption were excluded. Patients with Hormonal changes especially in women were excluded. Patients with Pancreatitis, massive blood transfusion, renal failure, septic shock, hyper-phosphatemia were excluded. Patients on Medication like phenytoin, rifampicin, phenobarbitone and corticosteroid were excluded. Patients already on calcium supplements were excluded.

Study procedure: All the 83 patients included were allowed to submit informed consent to participate in the study; and in case of children below 18 years, the parents gave the informed consent. A thorough clinical examination of the patients was undertaken. Laboratory investigations included were the surgical profile and serum calcium, vitamin D, and parathyroid hormone (PTH) levels. Ultrasound examination of the Thyroid gland and Neck was undertaken in all.

Total thyroidectomy: The entire thyroid is removed without retaining any tissues.

Procedure: It was done under General Anaesthesia. A Horizontal skin crease incision is put two finger breadths above the supra-sternal notch. Sub-platysmal flap is raised. A midline vertical incision was taken to open the deep cervical fascia. Strap muscles were retracted. Dissection is done through the loose areolar tissue between thyroid and carotid sheath. The superior pedicle was exposed and ligated. Inferior pedicle was also identified, ligated and cut. Both blunt and sharp dissections were used to expose the recurrent laryngeal nerve and parathyroid glands. Ligation of inferior thyroid artery or its branches close the gland avoid injury to artery of parathyroid was done. Opposite lobe was also dissected similarly. The entire gland is removed without causing injury to the posterior structures. Post-surgery Thyroid gland specimens were subjected to Histopathology examination and necessary protocols were followed up based on the final diagnosis. During the post-operative period, clinical assessment was done combined with estimation of serum calcium values. Hypocalcaemia was defined as a serum calcium level of <2.00 mmol/L. The collected data included the demographic details, specific type of operative procedure that was undertaken, patients' serum calcium levels, Clinical symptoms and signs of Hypocalcaemia, Laboratory reports of low serum calcium levels, the day on which the Hypocalcaemia was detected, the day of recovery

from Hypocalcaemia (Normocalcemia) based on laboratory report and Length of Hospital Stay.

Post-operative Protocol: Laboratory investigations included were estimated corrected calcium and PTH levels at 4 to 6 hours postoperatively and again on day 1 and on day 2 postoperatively.

Treatment Protocol: Intravenous Calcium Gluconate (10 ml of 10% Calcium Gluconate diluted in 250 ml of NaCl over 30 minutes) for patients who have a corrected serum calcium level of <2.00 mmol/L and severe symptoms was undertaken. If the patients were symptomatic on the next day or corrected serum calcium level of <2.00 mmol/L, chewable Tablet Calcium Carbonate 500-mg three times a day and a single dose of 1 µg of vitamin D3 were given. If there were no symptoms and or corrected serum calcium level of >2.00 mmol/L, the patient was considered for safe discharge with an instruction to use chewable Tablet Calcium Carbonate 500-mg three times daily.

Schedule for reduction of outpatient supplemental therapy: Calcium levels were estimated at 6 weeks postoperative period. Calcium carbonate dosage was reduced over next 3 weeks. Original dosage of Calcium Carbonate was resumed whenever the symptoms recur. To estimate the calcium level weekly and if hypocalcaemia persists, check the calcium level is normal or not. Reduce vitamin D and correct the magnesium level dosage to 0.5 µg and then to 0.25 µg over 4 weeks. Check the serum calcium level every 2 weeks and then at 6 weeks after stopping supplemental therapy. If the patient becomes symptomatic original regimen restarted.

Statistical Analysis: continuous variables were expressed as mean, + or – SD, categorical variable were expressed as frequencies and percentages. Student's test (paired t test) was used to analyze the statistical difference in parametric data. Chi-square test was applied for categorical data. A "p" value of less than 0.05 was considered as statistically significant.

Results

Among the 83 patients included in this study, 10 (12.04%) patients were aged between 15 and 25 years, 14 (16.86%) patients were aged between 26 and 35 years, 27 (32.53%) patients were aged between 36 and 45 years, 23 (27.71%) patients aged between 46 and 55 years and 09 (10.84%) patients were aged between 56 and 65 years. (Table 1) Majority of the patients belonged to the age group intervals of 36 to 45 and 46 to 55 years; 58 (69.87%). There were 61 (73.49%) females and 22 (26.50%) male patients among the total 83 patients in the study. The male to female ratio was 1:2.77 (Table 1)

Table 1: Age and Gender Distribution of Study Population (N-83)

Age Interval	Frequency	Percent	Gender	
			Female- 61 (73.49%)	Male- 22 (26.50%)
	Number	%	Number	Number
15-25	10	12.04	07 (08.43%)	03 (03.61%)
26-35	14	16.86	10 (12.04%)	04 (04.81%)
36-45	27	32.53	20 (24.09%)	07 (08.43%)
46-55	23	27.71	18 (21.68%)	05 (06.02%)
56-65	09	10.84	06 (07.22%)	03 (03.61%)
Total	83	73.49	61 (73.49%)	22 (26.50%)

The youngest patient was aged 16 years and the eldest one was aged 65 years. The mean age was 42.43, median was 42.00 and the mode was 39 in this study. Standard deviation was 11.356 **(Table 2).**

Table 2: Showing the Mean, median and mode and SD of the study population (n-83)

Age	Values
Mean	42.43
Median	42.00
Mode	39
Std. Deviation	11.356
Minimum Age	16
Maximum Age	65

The mean pre-operative serum calcium levels of the study population were assessed and it was found to be as 9.274+0.627. **(Table 3)**

Table 4: Pre-Operative Serum Calcium Levels

Mean	9.2745
Median	9.3250
Std. Deviation	.627

Among the 83 patients, the pre-operative diagnosis was Follicular Neoplasm in 11 (13.25%) patients, MNG with retrosternal extension was found in 10 (12.04%) patients, Euthyroid and multinodular Goitre was observed in 47 (56.62%) patients, Papillary carcinoma thyroid was noted in 09 (10.84%) patients and Treated MNG was found in 06 (07.22%) patients. (Table 5) Out of all the diseases of the Thyroid in the present study, Euthyroid MNG was the commonest diagnosis accounting to 56.62%, followed by follicular neoplasm and papillary carcinoma together accounting for 20/83 (24.09%), (Table 5).

Table 5: Pre-Op Diagnosis Made Among the Study Population (N-83)

Pre-operative Diagnosis	Frequency	Percent
Follicular Neoplasm	11	13.25
Mng With Retrosternal Extension	10	12.04
Euthyroid Multinodular Goitre	47	56.62
Papillary Carcinoma Thyroid	09	10.84
Treated Toxic Mng	06	07.22
Total	83	100

The histopathology of the lesions of Thyroid in the present study showed that 89.15% of the patients presented with MNG, followed by Toxic MNG and MNG with lymphocytic Thyroiditis. (Table 6) The incidence of Hypocalcaemia was 14/83 (16.86%) in Multinodular Goiter with Lymphocytic Thyroiditis, 26/83 (31.32%) among the MNG patients and 03 (03.61%) of the Papillary carcinoma patients. (Table 6)

Table 6: Showing the Histopathology Diagnosis in the Study Population (N-83).

Diagnosis	Frequency	Percent	Hypocalcaemia
Mng With Lymphocytic Thyroiditis	27	32.53	14
Multinodular Goitre	47	56.62	26
Papillary Carcinoma	09	10.84	03
Total	83	100	43 (51.80%)

The post-operative Patients developing Hypocalcaemia on the first post-operative day were 13 (15.66%), on the second post-operative day were 19 (22.89%), on the third post-operative day were 23 (27.71%), on the fourth post-operative day were 08 (09.63%), (Table 7).

Table 7: Showing the incidence of Hypocalcaemia during the Post-operative period from Day 1 to 4 (n-83)

	Frequency	Percent
POD1	13	15.66
POD2	19	22.89
POD3	23	27.71
POD4	08	09.63

The number of patients showed clinical symptoms and signs were observed and found that Peri-oral mucosal numbness was complained by 18 (21.68%) patients, Paraesthesia was complained by 17 (20.48%) of the patients and Carpopedal spasm was observed in 03 (03.61%) patients (Table 8). The appearances of the symptoms during the immediate postoperative period on different days (0 to 04 days) were tabulated in the Table 8. On the day 2 post-operative period the incidence of transient ischemia was noted in 07.83 (08.43%) of the total 83 patients. (Table 8)

Table 8: Incidence of Clinical Symptoms and Signs among Study Population (n-83).

Symptoms and Signs	Frequency (out of 83 patients)				percentage
	Day 1	Day 2	Day 3	Day 4	
Peri-oral numbness- 18	0	04	06	08	21.68%
Paraesthesia - 17	0	03	09	05	20.48%
Carpopedal spasm- 03	0	0	01	02	03.61%
Total	**0**	**07**	**16**	**15**	100%

The development of Hypocalcaemia and its effects in different age groups was analyzed and it was found that the clinical symptoms and signs were predominantly found in the age group intervals of 36 to 45 and 46 to 55 years age intervals accounting to 25 (30.12%) of the patients (Table 9). Overall 38 (45.78%) patients out of 83 presented with clinical symptoms and signs.

Table 9: Incidence of Clinical Symptoms and Sign among Different Age Groups (n-83)

		Total Thyroidectomy patients	Presence of clinical Sign	None
Age group	15-25	10	03	07
	26-35	14	08	06
	36-45	27	17	10
	46-55	23	08	15
	56-65	09	02	07
Total		**83**	**38 (45.78%)**	**45 (54.21%)**

The pre-operative calcium values and calcium levels on the post-operative day one were compared using the independent 't test' and it was found that there was a significant difference between the post and pre-op values ($p<0.05$), (Table 10). On comparing the post-operative calcium levels on the day 2nd, 3rd and 4th with the appearance of any of the clinical signs and symptoms, it was observed that the clinical signs developed in those with lower serum Calcium levels which was statistically significant with p value at 0.001.
(Table 10)

Table 10: Comparison of Pre and Post-Operative Serum Calcium levels Using Paired 'T Test'

Paired Samples Statistics				
	Mean	N	Std. Deviation	P Value
PRE-OP Serum Calcium	9.2745	83	.62741	0.001
Serum Ca+ ion POD1	9.0553	83	.60851	0.001
No signs		83		
Serum Ca+ ion POD 2				
No signs	8.6850	**76**	.44717	
Peri-oral Numbness	6.1000	**04**	.51962	**0.001**
Paraesthesia of extremities	5.7213	**03**	.61763	
Carpopedal spasm	4.3872	**00**	.57820	
Total	8.5631	**83**	--	--
Serum Ca+ ion POD 3				
No signs	8.4430	**67**	.24231	
Peri-oral Numbness	7.7800	**06**	1.24451	**0.001**
Paraesthesia of extremities	7.5900	**09**	.58029	
Carpo-pedal spasm	4.1890	**01**	.64665	
Total	8.0800	**83**	--	--
Serum Ca+ ion POD 4				
No signs	8.2750	**68**	.35940	
Peri-oral Numbness	8.1000	**08**	.46112	**0.001**
Paraesthesia of extremities	6.7767	**05**	.72145	
Carpopedal spasm	7.0237	**02**	.48327	
Total	7.6912	**38 (45.78%)**	.83258	--

The Hospital stay in days was calculated for all the 83 patients and a comparison was made between those who did not develop Hypocalcaemia and those who developed it.

The Mean values of Hospital stay in days were tabulated in the Table 11. It was found that earlier the development of Hypocalcaemia shorter was the Hospital stay. The Mean Hospital stay was statistically lower and significant in the patients without developing Hypocalcaemia than those developing Hypocalcaemia (p value was 0.00 which was <0.05).

Overall 63 (75.90%) patients presented with low serum calcium levels and without Hypocalcaemia in 20 (24.09%) patients which was significant statistically with p value at 0.001. (Table 11)

Table 11: Showing the Mean Hospital stay in patients developed Hypocalcaemia during different days of the Post-operative period (n-83; 63 with Hypocalcaemia). (POD-Post operative Day)

Observation	Frequency	Percent	Mean Hospital Stay Days
POD1	13	15.66	4.218±1.08
POD2	19	22.89	4.910±1.66
POD3	23	27.71	5.314±2.35
POD4	08	09.63	5.880±1.10
Total	**63 (75.90%)**	**100**	**4.310±0.35**
Without Hypocalcaemia	**20 (24.09%)**	**24.09**	**3.211±0.75**

Discussion:

The present study was undertaken to assess the occurrence of hypocalcaemia following Total thyroidectomy. To study various clinical presentations of post total thyroidectomy hypocalcaemia, day of appearance of its symptoms or fall in serum (Ca+) levels, correlation of the symptoms with the serum calcium levels, correlation of post total thyroidectomy hypocalcaemia with other indications of total thyroidectomy and its prevalence in relation to the age and gender in a tertiary care centre in North Kerala. The study was conducted among 83 patients who had undergone Total Thyroidectomy surgeries. There was a significant reduction in serum calcium levels in these patients after the Total Thyroidectomy. The mean pre-operative calcium level was found to be 9.25 mg/dl among the study population. The mean post-operative calcium level was 9.05 mg/dl on the Day 1. The mean values of serum calcium are slightly higher when compared to that reported by Nair CG et al. They had observed that the mean preoperative serum calcium of 8.9 mg/dl and a mean postoperative calcium of 8.25 mg/dl. [14] Among the 83 patients of the study diseases of the Thyroid in the present study, Euthyroid MNG was the commonest diagnosis accounting to 56.62%, followed by follicular neoplasm and papillary carcinoma together accounting for 20/83 (24.09%), MNG with retrosternal extension was found in 10 (12.04%) patients (Table 5). The histopathology of the lesions of Thyroid in the present study showed that 89.15% of the patients presented with MNG, followed by Toxic MNG and MNG with lymphocytic Thyroiditis. (Table 6) The incidence of Hypocalcaemia was 14/83 (16.86%) in Multinodular Goiter with Lymphocytic Thyroiditis, 26/83 (31.32%) among the MNG patients and 03 (03.61%) of the Papillary carcinoma patients. (Table 6) This is in agreement with the epidemiological studies on thyroid swellings in the Indian scenario.

Recent population-based studies in India have found out that nearly 12% of adult populations in India are having a palpable Goiter. This may be attributed to the iodine deficiency. Now research has shown that iodine deficiency is an important public health problem not only in Himalayan and Sub-Himalayan regions, but also most of the regions in India. This leads to decompensate Hypothyroidism in many people. [15] In the present study the post-operative Patients developing Hypocalcaemia on the first post-operative day were 13 (15.66%), on the second post-operative day were 19 (22.89%), on the third post-operative day were 23 (27.71%), on the fourth post-operative day were 08 (09.63%), (Table 7). Bentrem DJ, Rademaker A and Angelos P [16] had evaluated from their study that the, timed serum calcium levels in patients following Total Thyroidectomy or Parathyroidectomy Hypocalcaemia in 15% of their cases. But, they had observed Hypocalcaemia, 22 hours after Total Thyroidectomy surgery. They had put the criteria for postoperative hypoparathyroidism as presence of clinical symptoms with a total calcium value of less than 7.2 mg/dL, or an ionized calcium value of less than 1.0 mmol/L. [16]. In another similar study by Abboud B, Sargi Z et al [17], 16% patients were found to have Hypocalcaemia with 04% being symptomatic. These symptomatic patients required vitamin D, calcium or both for 2-6 weeks. Overall 63 (75.90%) patients presented with low serum calcium levels and without Hypocalcaemia in 20 (24.09%) patients which was significant statistically with p value at 0.001. (Table 11) The Mean Hospital stay was statistically lower and significant in the patients without developing Hypocalcaemia than those developing Hypocalcaemia (p value was 0.001 which was <0.05). (Table 11) Nair CG et al [14] found the incidence of Hypocalcaemia to be 23.6% among their post Total Thyroidectomy patients. Permanent Hypocalcaemia was diagnosed in 01.61%. The onset of Hypocalcaemia symptoms was found to be delayed up to the third postoperative day in their study. This delayed onset of Hypocalcaemia symptoms was similar to what was observed in the present study wherein the symptoms & signs of Hypocalcaemia and low serum calcium levels appeared after 24 hours. This implies that Hypocalcaemia can occur late in the postoperative period. This may be considered as the latent Hypocalcaemia. Sasson AR et al [18] had observed that among the 141 thyroid procedures, 49% were Total Thyroidectomy cases and 51% were thyroid lobectomies. The incidence of Hypocalcaemia was noted to be 06.6 %. This is a lesser incidence when

compared to what was noted in the present study which was 75.90% (Table 11). Sasson AR et al [18] also observed 52% of the Total Thyroidectomies were performed for malignant diseases of the thyroid; Incidental parathyroidectomy was found in 15% of the total cases. According to them, modified radical neck dissection was associated with an increased chance of unplanned Parathyroidectomy. But, the postoperative Hypocalcaemia was not found to be associated with the incidental Parathyroidectomy in their study. These findings may not be comparable to the findings in the present study, because there is a substantial difference in the proportion of patients with malignancies in both settings; malignant tumors in the present study occurred in 10.84% of the patients. The proportion of patients classified as developing post-operative hypocalcemia can vary in different study settings. The variations in the case definition criteria and characteristics of the study population mainly lead to these differences. Adopting different study designs can also result in varied incidence of hypocalcemia to be observed in different studies. Tredici et al. [19] observed that the proportion of patients developing Hypocalcaemia was found to be 50% in retrospective analysis while, it was 80% in the prospective series. But, the proportion of those developing symptomatic hypocalcemia was more in the retrospective assessment. In the present study, out of the total 83 patients, 38 (45.78%) patients developed symptomatic Hypocalcaemia (Table 10) which was similar to the study of Tredici et al [19]. Similar studies by Gac EP et al. in 2014 and Wingert et al. in 1986 [20,21] observed that the incidence of symptomatic Hypocalcaemia was lower when compared to this study. A comparison of the incidence of symptomatic hypocalcemia in present study and some other studies is given in table number 12 below.

Table 12: Comparison of incidence of symptomatic Hypocalcaemia in present study and similar other studies

Study	Incidence of Hypocalcaemia
Wingert et al. [21]	12.5%
Scanlon et al. [22]	20%
Gac EP et al. [20]	15%
Present study	**45.78%**

In present study, there were no clinical signs among the study population on the first post-operative day. But, by post-operative day 2, symptoms were started to develop in some of the patients. Peri oral numbness was the most commonly seen symptom on second, third and fourth post-operative days; 18/83 (21.68%) of the patients complained of this symptom. Paraesthesia of extremities was reported on second, third and fourth post-operative days; 17 17/83 (20.48%) of the patients complained of this symptom. But signs like Carpo-pedal spasm was reported on third and fourth post-operative days respectively in 03/83 (03.61%) patients (Table 10). Maximum number 16/83 (19.27%) of patients presented with clinical symptoms of Hypocalcaemia were seen on the third post-operative day. But, Bentrem DJ et al. [16] had observed symptomatic Hypocalcaemia even within 22 hours after the Total Thyroidectomy surgeries. In the present study most of the patients, 50/83 (60.24%) belonged to the middle age group intervals of 36 to 55 years. (Table 1) Majority of the patients i.e., 61 (73.49%) were females. (Table 1) Female gender was observed to be a risk factor for Hypocalcaemia by Abboud et al. [17]. Parathyroid auto-transplantation, raised free thyroxine levels and bilateral thyroidectomy were the other observed risk factors for Hypocalcaemia in Total Thyroidectomy patients. [17] More recent search was based on the predictive value of preoperative levels of serum calcium or parathyroid hormone. Garbutt L, et al et al. [23] suggested that the intra-operative parathyroid hormone levels were better predictors of post thyroidectomy Hypocalcaemia when compared to the serum calcium levels postoperatively. Such a prediction would help in identifying patients who might need intravenous calcium during the postoperative period. The development of Hypocalcaemia and its effects in different age groups was analyzed and it was found that the clinical symptoms and signs were predominantly found in the age group intervals of 36 to 45 and 46 to 55 years age intervals accounting to 25 (30.12%) of the patients (Table 9). Overall 38 (45.78%) patients out of 83 presented with clinical symptoms and signs. But, according to Nair CG et al, [14] the incidence of hypocalcemia was not affected by the age or gender. There was a significant difference observed in the post-operative serum calcium levels of those patients with clinical features and those without. The serum calcium level was lower among those with perioral numbness when compared to those without any features on second post-operative day. The pre-operative calcium values and calcium levels on the post-operative day one were compared using the independent ‘t test’ and it was found that there was a significant difference between the post and pre-op values ($p<0.05$), (Table 10). On comparing the post-operative calcium levels on the day 2nd, 3rd and 4th with the appearance of any of the clinical signs and

symptoms, it was observed that the clinical signs developed in those with lower serum Calcium levels which was statistically significant with p value at 0.001. (Table 10) These observations point towards the association of serum calcium levels with the clinical manifestations of hypocalcemia. These are in agreement with the findings from various perspective and retrospective records on the clinical features and serum calcium levels among these patients. [24] Chen et al, [25] concluded from their meta-analysis that the incidence of Hypocalcaemia was higher when the parathyroid gland function was badly affected. In addition, other factors predisposing to Hypocalcaemia after Total Thyroidectomy were, Vitamin D deficiency. There was a possibility of sudden increase in serum calcitonin levels because of manipulation of the gland during surgery. Another underlying mechanism is attributed to the "hungry bone syndrome" where calcium was being taken up by the skeletal system. Some etiological considerations apart from the above mentioned causes include post-operative alkalosis-induced hypocalcaemia resulting from hyperventilation triggered by postoperative pain, and dilutional hypocalcaemia [5].

All these factors may be contributing their parts to the development of hypocalcemia in post thyroidectomy patients rather than attributing the event to one particular cause or mechanism. Another critical factor is the amount of parathyroid gland retained after the procedure of thyroidectomy. As the amount retained becomes less, the chances of developing hypocalcemia are observed to be more. [5] This is in coherence with the known facts on the association of serum calcium level and presence of functioning parathyroid glands. The retention of at least one parathyroid gland is thought to be helpful in preventing permanent postoperative hypocalcemia. This fact was pointed out by Zedenius et al., [26] also. Zedenius et al [26] from their study on 100 cases of thyroidectomy concluded that permanent Hypo-Para thyroidism could be prevented by routinely transplanting at least one parathyroid gland into steronocleido-mastoid muscle. Transient Hypocalcaemia/ temporary hypocalcaemia usually resolves within 2 months and sustains maximum up to 6 months after the onset. Permanent hypocalcemia is the one that continues beyond 6 months of onset. [5] In the present study conducted prospectively and follow ip of the patients was done only up to a limited postoperative period of 18 months and hence cannot be concluded about incidence of permanent Hypocalcaemia. Prospective studies beyond 24 months after the surgical procedure only will be able to throw light into this aspect. The table 13 showed the incidence of transient and permanent hypocalcemia in various studies conducted. On the day 2 post-operative period of the present study, the incidence of transient ischemia was noted in 07.83 (08.43%) of the total 83 patients. (Table 8)

Table 13: Comparison of incidence of transient and permanent Hypocalcaemia in various studies conducted

Study	Incidence of transient hypocalcemia	Incidence of permanent hypocalcemia
Thomusch et al. [27]	7.3%	1.5%
Fahmy et al. [24]	5.4-26%	0.5-24%
Karamanakos et al [28]	6.9-46%	0.4-33%
present study	**07- 08.43 (On2nd Post OP Day)**	**Could not be assessed**

In present study, incidence of symptomatic hypocalcemia was observed to be higher among those with a preoperative diagnosis of multinodular goiter, in comparison with those with diagnoses of toxic multinodular goiter or papillary carcinoma. The histopathology of the lesions of Thyroid in the present study showed that 89.15% of the patients presented with MNG, followed by Toxic MNG and MNG with lymphocytic Thyroiditis. (Table 6)

The incidence of Hypocalcaemia was 14/83 (16.86%) in Multinodular Goiter with Lymphocytic Thyroiditis, 26/83 (31.32%) among the MNG patients and 03 (03.61%) of the Papillary carcinoma patients. (Table 6) Though, there was a difference observed in the incidence of symptomatic hypocalcemia among these groups, it was not statistically significant in contrary to the findings in some of similar prior literature. Burge et al in 1998 [29] observed that permanent hypocalcemia was seen more among those patients who underwent thyroidectomy for malignant thyroid swellings, while transient hypocalcemia was seen more among those who had a thyroidectomy for the diagnosis of Graves' disease. Similarly, according to Sakouti et al, [30] neck node dissection in thyroid malignancy was associated with postoperative hypocalcemia, but no such finding was observed by Noureldine et al in 2014 [31]. The absence of significant difference in incidence of symptomatic hypocalcemia between those with different preoperative diagnoses in the present study might be most probably due to the comparatively smaller sample size. A significant difference would have been observed if this factor was explored on a larger group. As per Wingert et al, [7] incidence of postoperative hypocalcemia was higher among patients with malignant thyoid

disease compared to its incidence among those with toxic goitre or multinodular Goiter. In present study, the significant reduction in the postoperative serum calcium level is evident.

This signifies the importance of need for monitoring the same. Kanis JA, Russell RG et al [32] had stressed serum calcium estimation as an effective predictor of hypocalcemia and the pointer to the need for a proper monitoring and timely correction of the same. Parathormone level estimation was recommended as a predictor of Hypocalcaemia by O Edafe et al in 2014. [33] This monitoring and corrective measures for hypocalcemia may have to be extended beyond the postoperative period. Patients with severe hypocalcemia may require calcium supplementation with or without Vitamin D3 for about 3-6 months as recommended by Kanis et al. [32]

Summary & Conclusions

Hypocalcaemia following Total Thyroidectomy remains a significant clinical challenge. The present study demonstrated a substantial incidence of post-operative Hypocalcaemia, with peak occurrence on the third post-operative day.

This finding underscores the importance of vigilant monitoring during the immediate post-operative period. The clinical manifestations of Hypocalcaemia were predominantly Perioral numbness and paraesthesia, affecting a considerable proportion of patients. Notably, these symptoms were more prevalent in the age groups of 36-45 and 46-55 years.

A statistically significant decrease in serum calcium levels was observed post-operatively, directly correlating with the development of clinical symptoms. These findings emphasize the critical role of early identification and management of Hypocalcaemia to mitigate patient discomfort and potential complications. Further research is warranted to explore the underlying mechanisms contributing to post-operative Hypocalcaemia and to identify potential predictive factors. This knowledge could lead to the development of targeted preventive strategies and optimize patient care.

In conclusion, the present study highlights the importance of regular serum calcium monitoring and early intervention in patients undergoing Total Thyroidectomy to prevent the development of symptomatic Hypocalcaemia and improve overall patient outcomes.

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