IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 12 Ver. IV (Dec. 2017), PP 34-49
www.iosrjournals.org

Clinical Study of Post Thyroidectomy Hypocalcemia

Dr K S Satya Vani[1],*Dr M Sri Sailaja Rani[2]
[1]*Dr K S Satya vani ,Associate Professor, General Surgery, Rangaraya Medical College, Kakinada,East Godavari Dist, Andhra Pradesh, India.*
[2]*Dr M Sri Sailaja Rani , Associate Professor, General Surgery, Rangaraya Medical College, Kakinada,East Godavari Dist, Andhra Pradesh, India.*
**Corresponding author:*Dr M Sri Sailaja Rani*

Abstract:
Background*: Hypocalcaemia following thyroid surgery is the most common complication following thyroid surgery. This study will evaluate the risk factors and predictors of hypocalcaemia either transient or permanent.*
Design*: Prospective analysis of 50 consecutive patients undergoing thyroid surgeries.*
Materials & Methods*: All patients undergoing any thyroidectomy in the department of general surgery were followed for a period of 3 months. The type of surgery, Histopathology and clinical diagnosis to predict the outcome of post-operative hypocalcaemia was validated. The influences of Patient factors, intra-operative identification of RLN and parathyroid were also observed.*
Results*: The overall prevalence of hypocalcaemia was 28% of which 12 patients had temporary and 2 had permanent hypocalcaemia. Only 12 patients developed clinical symptoms. Hypocalcaemia typically ensues during the early post-operative period (24-48 hrs). Hypocalcaemia was significantly associated with the type of surgery (P=0=0.0293), Histopathology (p=0.0312) and clinical diagnosis (p=0.0008). Age, Sex and identification of RLN and Parathyroid did not play a significant role in predicting the outcome of post-operative hypocalcaemia.*
Conclusion*: Hypocalcaemia either transient or permanent can be debilitating and lead to significant morbidity. Temporary hypocalcaemia is common after surgery for malignancies. Histopathology, clinical diagnosis and extent of surgical resection influence the outcome of hypocalcaemia. Early measurement of serum calcium and albumin levels can ensure early management and prevent complications of hypocalcaemia.*
Key words*: Hypocalcaemia, Hypoparathyroidism, Parathyroid, Thyroidectom*

Date of Submission: 02-12-2017 Date of acceptance: 09-12-2017

I. Introduction

Thyroid disorders are the second most common endocrinologic disorder following diabetes. An estimated population of 42 million in India are said to be suffering from thyroid disorders[1]. The nationwide relative frequency of thyroid cancer among all the cancer cases was 0.1 - 0.2%. Goitres are more common in the iodine deficient areas like the Himalayan belt. Thyroid dysfunction was common in women especially in the age group of 40-60 years[1,2].Thyroid operations have evolved from the 18th century to the present minimal access surgeries, and are being performed on a day care basis. Surgery has been offered for various thyroid disorders especially malignancy, as a definitive remedy. Thyroid operations have been classified based on the amount of tissue left over following resection. Each type of thyroid surgery has its own advantages and disadvantages, associated with some amount of morbidity.Hypocalcaemia is a well-recognized complication of thyroid operation which can be either transient or permanent. Hypocalcaemia is defined as serum calcium less than the normal levels with one or more symptoms. Transient hypocalcaemia usually resolves within a week post-operatively. Patients dependent on calcium supplements to maintain normocalcaemia beyond three months are labelled permanent hypocalcaemia.According to literature the prevalence of temporary hypocalcaemia ranges from 1.6-23% and permanent hypocalcaemia 0.77-4.2%[4]. Hypocalcemia usually occurs in the early post-operative period within 72 hours and resolves spontaneously in the 5th- 7th post-operative day. It is ideal to supplement calcium either orally or intravenously during this critical phase. For patients who progress to permanent hypocalcaemia Vitamin D3 supplement along with magnesium is required.

This study will consider the possible risk factors for post-operative hypocalcaemia and record its prevalence following various thyroid surgeries. Correlation of the laboratory and symptomatic hypocalcaemia, appearance of symptoms were also observed during the post-operative period.

II. Aims And Objectives

1) To Record the incidence of post-thyroidectomy hypocalcaemia
2) To correlate blood calcium levels with symptoms of hypocalcaemia
3) To find out the type of hypocalcaemia whether temporary or permanent
4) To assess the risk factors for development of hypocalcaemia.

III. Subjects And Methods

This was a prospective observational study, which conducted at the Tertiary care teaching HospitaI, over a one year period.The Institutional Medical Ethics Committee approved this study from February 2016 until April 2017. We enrolled patients undergoing various thyroid operations only in the Department of General Surgery. Written informed consent was obtained from the patient for inclusion in this study.

We excluded all patients with:

1. Pancreatitis
2. Nephrotic syndrome
3. Chronic renal failure
4. Previous radiation to neck
5. Malabsorption
6. Pre-operative low serum calcium

3.**1 Inclusion criteria:**

All patients with a normal pre-operative calcium level and undergoing any thyroid surgery in the Department of General Surgery were included in this study.

IV. Methodology

Subjects who satisfy the inclusion criteria and voluntarily agree to be pact of the study were assessed for surgery and assessment of post-operative hypocalcaemia was done. A thorough clinical examination was performed, followed by blood investigations and imaging studies.

The initial assessment included:

4.1 Haematocrit

2. Thyroid Function tests:

1. Free T3
2. Free T4
3. TSH

4.2 Serum Calcium (Total) and Albumin

4. 3Renal functions by:

a. Serum Urea, Creatinine
b. Serum Electrolytes.
5. Indirect Laryngoscopy to check Vocal cords
6. Ultrasound of Neck
7. X-Ray Neck: AP & Lateral
8. FNAC of thyroid (Blind or USG Guided)

After initial assessment of patient for thyroid status and based on FNAC reports, the type of thyroidectomy was planned and patients were worked for surgery. Patients were followed for clinical signs of hypocalcaemia and also by laboratory assessment after thyroidectomy.

Clinical assessment:

Chvostek's Sign

Elicitation: Tapping at a point just anterior to the tragus over the anatomical position of Facial nerve, just below the zygomatic bone.

Positive response: Twitching of the ipsilateral perioral facial muscles, suggestive of neuromuscular excitability.

A similarly Chvostek Il phenomenon, can be produced by tapping on a different location of the face. This point is located on the line joining the zygomatic prominence and the corner of the mouth, one third distance from the zygoma[3].

Trousseau's sign

Elicitation: Inflating a sphygmomanometer cuff 20 mm of Hg above systolic blood pressure for not more than three minutes.

Positive response: Muscular contraction including flexion of the wrist and metacarpophalangeal joints, hyperextension of the fingers, and flexion of the thumb and the palm, suggestive of neuromuscular excitability[3].

Serum Calcium and Albumin will be monitored in Post-operative period 6, 24 and 48 hours and values will be repeated after a month of surgery and 3 months after surgery during follow up period.
Calculation 1
Corrected calcium = Serum Calcium / (0.6 + (Total Protein/8.5))
Calculation 2
Corrected Calcium = Serum Calcium + ((Normal Albumin - Serum Albumin) x 0.8)
Where normal albumin is often 4.0
Conversion used:
Calcium (mg/dL) x 0.25 = Calcium (mmol/L)
Albumin (g/dL) x 10 = albumin (P/L)

V. Drugs Used For Hypocalcaemia:

Calcium supplements were given to patients post-operatively and continued till patient attained normocalcaemia. For patients with permanent hypocalcaemia vitamin D3 supplements were added.
Inj Calcium Gluconate
Generic Name: Calcium Glucaonate
Route Of Administration: Intravenous
Dosage And Timing: 1-2 Ampoules Of 10% Intravenous Calcium Gluconate Over 10 Minutes
Trade Name: Calcium Gluconate Inj Ip
Tab Calcium
Generic Name: Calcium Carbonate
Route Of Administration: Oral
Dosage And Timing: 1500 Mg/Day In Three Divided Doses
Trade Name: Tab. Shelcal
Tab Vitamin D3
Generic Name: Vitamin D3
Route Of Administration: Oral
Dosage And Timing: 0.5 Mg Once Daily
Name: Alpha D3
Magnesium Supplements if required.
Calcium is administered carefully in patients taking Digoxin.

VI. Statistical Methods

SPSS software version 16 was utilised for statistical analysis and Chi-square test was employed to test the statistical significance of association between two discrete test variables (P=0.05). The variables analysed were as follows:
1. Age
2. Sex
3. Clinical diagnosis
4. Type of thyroidectomy
5. Identification of RLN
6. Identification of parathyroid
7. Histopathology

Other variables analysed were the clinical significance of symptomatic an laboratory hypocalcaemia, appearance of symptoms on post operative day. TV prevalence of symptomatic and asymptomatic hypocalcaemia was also compared.

VII. Results

A total of 50 patients undergoing thyroidectomy were included in this study. There were 42 females (84%) and 8 males (16%). There was a predominance of female when compared to male patients in the ratio of 5.25 : 1. (Table 1)Out of 50 patients 14 (28%) were between the age group of 20-29 years. 15 (30%) patients were in the age group of 30-39 years. 9 (18%) patients were in the age group of 40-49 years. 7 (14%) patients were within 50-59 years. There were 3(6%) patients in the age group of 60-69years and only 2 (4%) patients above 70 years. The mean age of the patients was 39.08 years (range: 20-80years) and median age was 36 years. (Table 2)Malignant thyroid disease was diagnosed in 11 patients (22%) and the rest 39 patients (78%) were diagnosed to have benign thyroid pathology. (Table 3)50 patients underwent different types of thyroidectomies for the above clinical diagnosis. 16 patients (32%)nderwent hemi-thyroidectomy either right or left along with or without identification of parathyroid and RLN on the same side. 15 patients (30%) underwent total

thyroidectomy as primary surgery. Central neck dissection was not done in any of the patients. Near total thyroidectomy was performed on 10 patients (20%) and sub-total thyroidectomy on 4 patients (8%). 5 patients (10%) underwent re-surgery, One of the patients had a recurrent MNG. The rest of the patients were diagnosed with malignancy during primary surgery and underwent completion thyroidectomy. (Table 4)The parathyroid glands were identified intra-operatively and every attempt to preserve the gland and its vascular supply was made. Parathyroid glands were identified in a total of 41 patients (82%). Parathyroid glands could not be identified in 9 patients (18%). All 4 glands were identified and preserved in only 2 patients. (Table 5)

The Recurrent Laryngeal Nerve was identified in a total of 35 patients (70%) either unilaterally or bilaterally. The recurrent laryngeal nerves were identified from inferior to superior method and were well preserved. RLN could not be identified in 15 patients (30%). No deliberate attempts were made to dissect the nerve which could lead to nerve injury. (Table 6)The overall prevalence of hypocalcaemia in the study was 14 (28%). Two patients (4%) progressed to permanent hypocalcaemia. The symptoms improved from the 5th to 7th post-operative day in the rest of the patients 12(24%) labelled as temporary hypocalcaemia. (Table 7)Of 14 patients who developed hypocalcaemia, the measured serum calcium was below normal in all 14 patients. But only 42 patients (85.7%) had clinical features suggestive of hypocalcaemia. (Table 8)

Based on the final reports of histopathology there were 19 patients (38%) with a diagnosis of malignant thyroid disorder. 12 patients (24%) were diagnosed with Papillary carcinoma and 5 patients (10%) had follicular carcinoma. There was 1 patient (2%) with anaplastic carcinoma and 1 patient (2%) with medullary carcinoma of thyroid. The rest 31 patients (62%) showed a benign picture on histological examination. Sixteen patients (32%) were diagnosed as colloid goitre and 11 patients (22%) as multi-nodular goitre. Three patients (6%) had hashimotos thyroiditis and one patient (2%) had a toxic goitre (Table 9)Of the 14 patients who developed hypocalcaemia the appearance of hypocalcaemia was significantly within 24-48 hours except for one patient who developed hypocalcaemia on the third post-operative day. There was no onset of hypocalcaemia beyond 72 hours. 5 patients (35.7%) out of 14 had an early onset of laboratory hypocalcaemia within 24 hours of which only 4 developed clinical symptoms. 8 patients (57.14%) developed both clinical and laboratory hypocalcaemia within 24-48 hours in the post-operative period. (Table 10)

Based on their age, patients were subdivided into two groups. There were 39 cases in the group below 50 years out of which 6 patients (50%) developed temporary hypocalcaemia and 1 patient developed permanent hypocalcaemia. There were 11 cases above 50years old out of which 6 patients (50%) developed temporary and 1 patient developed permanent hypocalcaemia. The age of the patient did not influence the outcome of hypocalcaemia statistically (P=0.2999). (Table 11)The female : male ratio in the study was 5.25 : 1. Of the 42 females who underwent thyroidectomy, 10 patients (83.3%) developed temporary hypocalcaemia. Only 2 patients (16.6%) in the male group developed temporary hypocalcaemia. Permanent hypocalcaemia was observed only in the female patients. Results were not statistically significant for sex of the patient (P=0.82), (Table 12)In our study 7 patients (63.7%) out of 11 in whom a clinical diagnosis of malignancy was made developed only temporary hypocalcaemia. None of them developed permanent hypocalcaemia. Of 39 patients in whom a benign diagnosis was made 5 (12.8%) developed temporary hypocalcaemia and 2 developed permanent hypocalcaemia. Chi square test showed a statistical significance between the clinical diagnosis and the outcome of hypocalcaemia (P- 0.0008). (Table 14)Patients were subdivided into 5 groups based on the type of surgery they underwent. None of the patients in the Sub-Total or Hemi-thyroidectomy group developed hypocalcaemia. Among the 15 patients who underwent total thyroidectomy, 4 patients (33.3%) developed temporary and 2 patients developed permanent hypocalcaemia. In the near-total group 5 patients (41.6%) out of 10 developed temporary hypocalcaemia. None of them developed permanent hypocalcaemia. The results were statistically significant when related to type of surgery (P=0.0293). (Table 15)The parathyroid gland was identified and preserved in a total of 41 patients. In the group with PTG identification 9 patients (75%) developed temporary and 1 developed permanent hypocalcaemia. In the group with PTG non-identification only 3 patients (25%) of the 9 developed temporary hypocalcaemia and 1 developed permanent hypocalcaemia. There was no statistical significance between PTG identification and development of post-operative hypocalcaemia (P=0.3332). (Table 16)Out of 35 patients in whom the RLN was identified 10 (83.3%) developed temporary and 2 patients developed permanent hypocalcaemia. In the group of patients in whom RLN was not identified only 2 patients (16.7%) developed temporary hypocalcaemia and none of them developed permanent hypocalcaemia. The values were statistically insignificant (P 0.6369). (Table 17)Based on the histopathology the patients were divided into two groups, either benign or malignant thyroid. Out of 31 patients who had a benign pathology, 3 patients (25%) developed temporary hypocalcaemia and 2 patients developed permanent hypocalcaemia. Out of 19 patients who were diagnosed with malignant pathology 9 patients (75%) developed temporary hypocalcaemia. There was no incidence of permanent hypocalcaemia in this group of patients. (Table 18)

VIII. Tables And Figures

Table 1: Sex wise distribution of patients

Sex	**No. Of Patients**
Female	42 (84%)
Male	8 (16%)
Total	**50 (100%)**

Figure 1: Sex wise distribution of patients

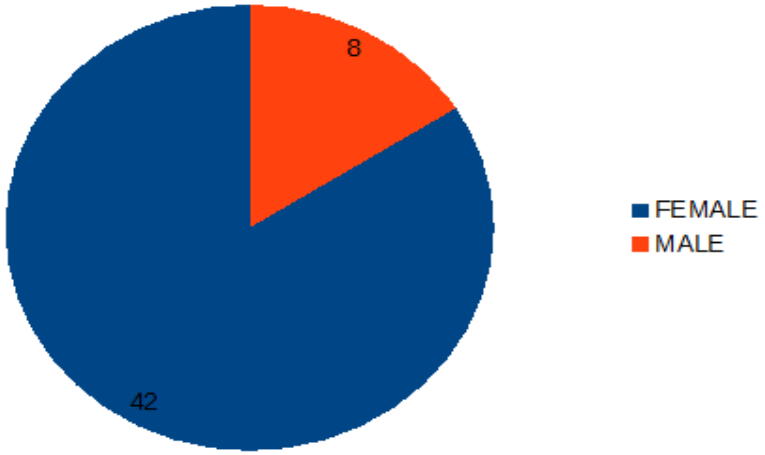


Table 2: Age wise distribution of patients

AGE	**NO. OF PATIENTS (%)**
20-29	14 (28)
30-39	15 (30)
40-49	9 (18)
50-59	7 (14)
60-69	3 (6)
>70	2 (4)
TOTAL	**50 (100)**

Figure 2: Age wise distribution of patients

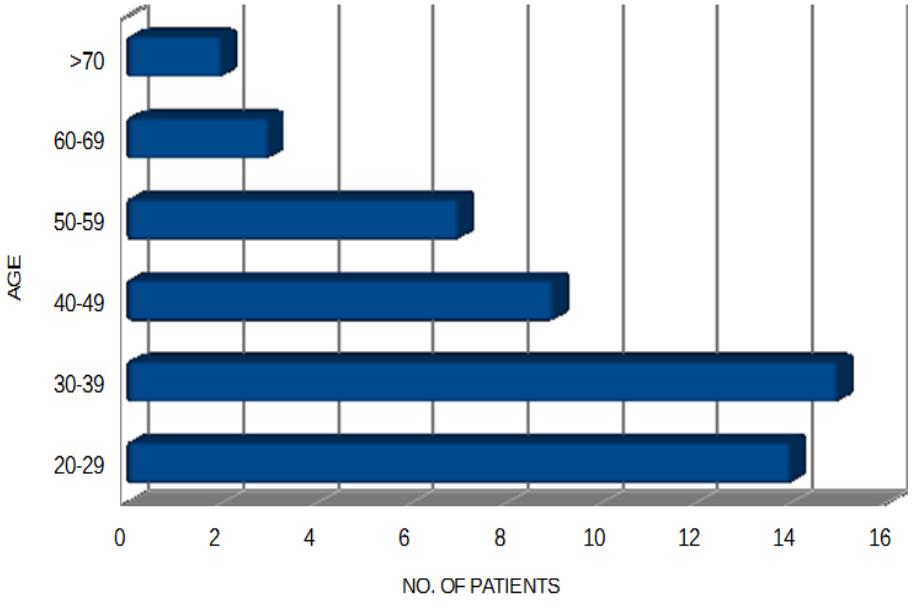


Table 3: Distribution of patients based on clinical diagnosis

Clinical Diagnosis	**No. Of Patients (%)**
Carcinoma	11 (22)
Benign	39 (78)
Total	50 (100)

Figure 3: Distribution of patients based on clinical diagnosis

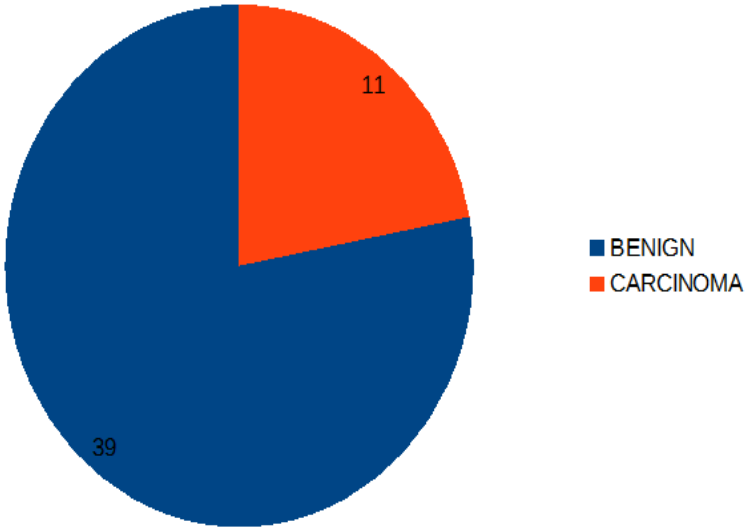


Table 4: Surgery wise distribution of patients

Type Of Surgery	No. Of Patients (%)
Total Thyroidectomy	15 (30)
Near Total Thyroidectomy	10 (20)
Sub Total Thyroidectomy	4 (8)
Hemi-Thyroidectomy	16 (32)
Reoperative	5 (10)
Total	50 (100)

Figure 4: Surgery wise distribution of patients

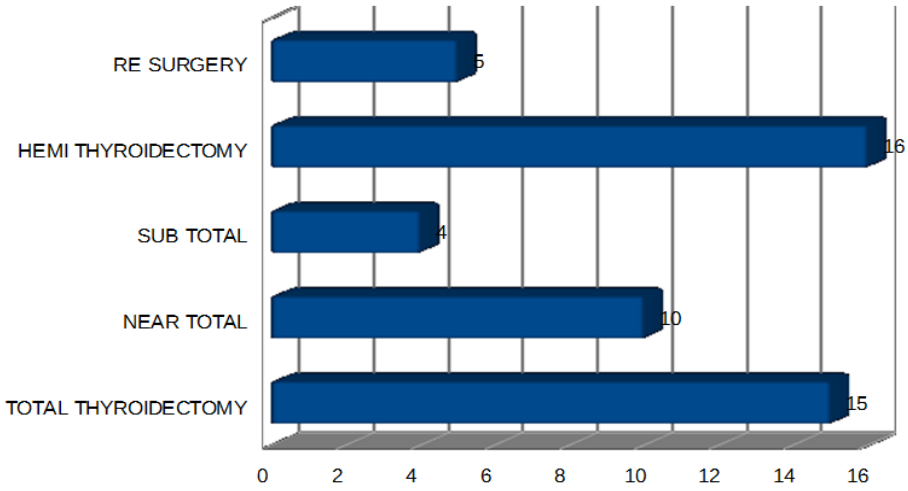


Table 5: Distribution of patients based on identification of PTG

Identification Of Parathyroid	Total (%)
Yes	41 (82)
No	9 (18)
Total	50 (100)

Figure 5: Distribution of patients based on identification of PTG

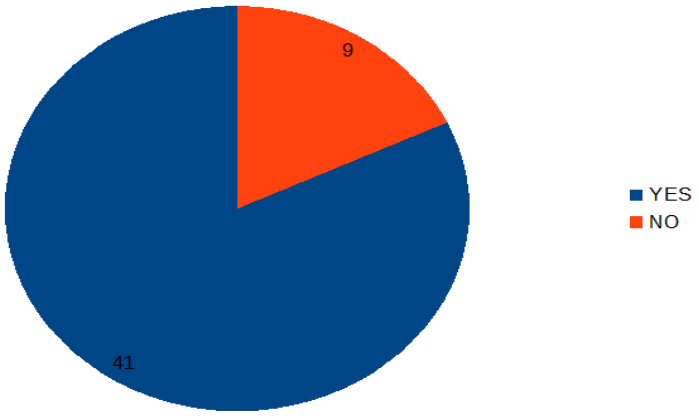


Table 6: Distribution of patients based on identification of RLN

Identification Of Rln	No. Of Patients (%)
Yes	35 (70)
No	15 (30)
Total	50 (100)

Figure 6: Distribution of patients based on identification of RLN

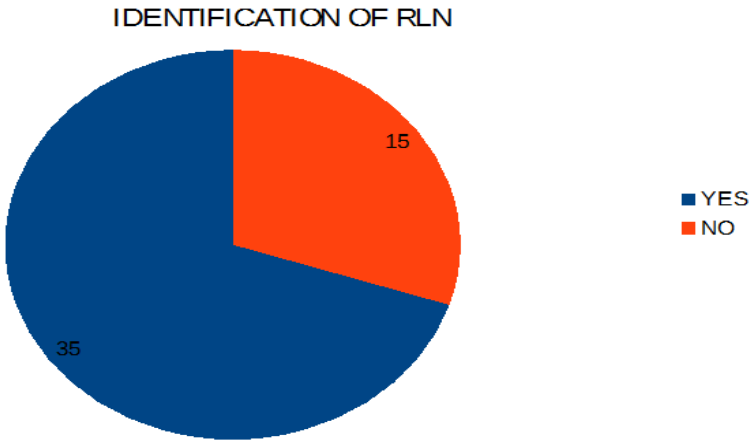


Table 7: Distribution of patients based on type of hypocalcemia

Hypocalcemia	No. Of Patients
Temporary	12 (85.7)
Permanent	2 (14.3)
Total	14 (100)

Figure 7: Distribution of patients based on type of hypocalcemia

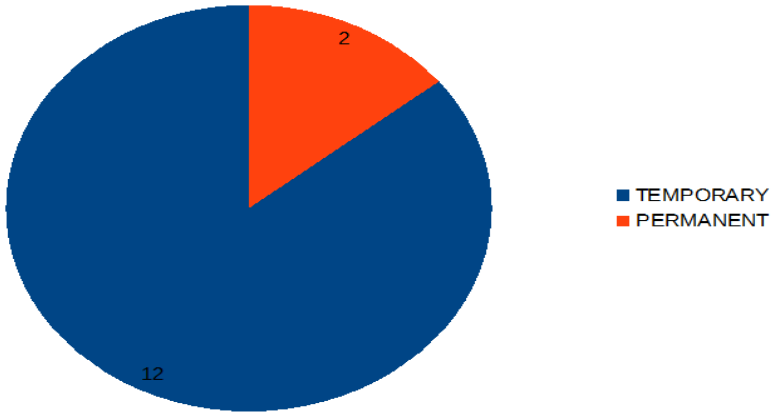


Table 8: Symptom wise distribution

Hypocalcemia	No. Of Patients (%)
Symptomatic	12 (85.7)
Asymptomatic	2 (14.3)
Total	14 (100)

Figure 8: Symptom wise distribution

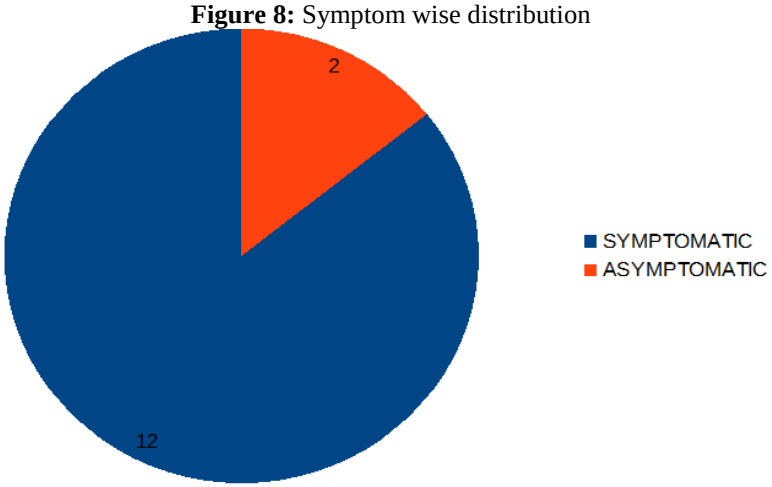


Table 9: Distribution of patients based on histopathology

Histopathology	No. Of Patients (%)
Colloid Goitre	16 (32)
Papillary Carcinoma	12 (24)
Multinodular Goitre	11 (22)
Follicular Goitre	5 (10)
Hashimoto	3 (6)
Toxic Goitre	1 (2)
Medullary Carcinoma	1 (2)
Anaplastic Carcinoma	1 (2)
Total	50 (100)

Figure 9: Distribution of patients based on histopathology

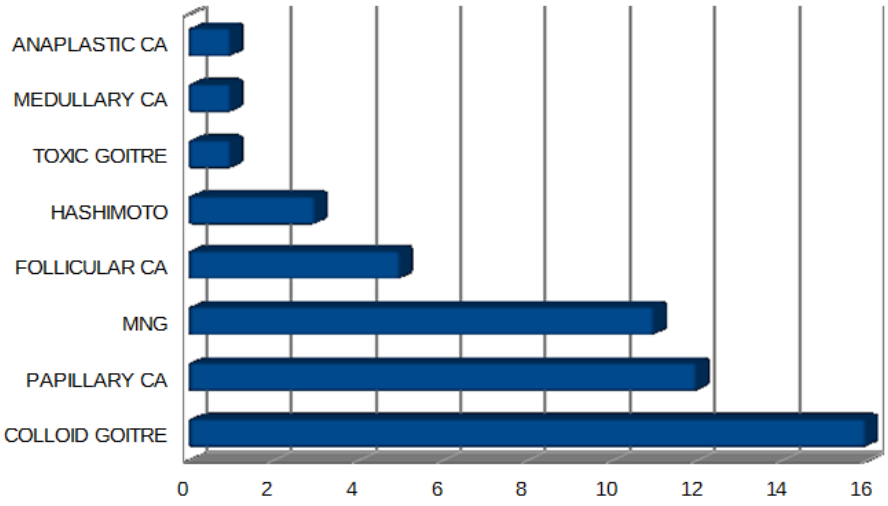


Table 10: Onset of climical and laboratory hypocalcemia post operatively

Appearance Of Hypocalcemia	Laboratory	Clinical
<24 Hrs	5 (35.7%)	4 (33.3%)
24-48 Hrs	8 (57.14%)	8 (66.7%)
48-72 Hrs	1 (7.1%)	0
>72 Hrs	0	0

Figure 10: Onset of climical and laboratory hypocalcemia post operatively

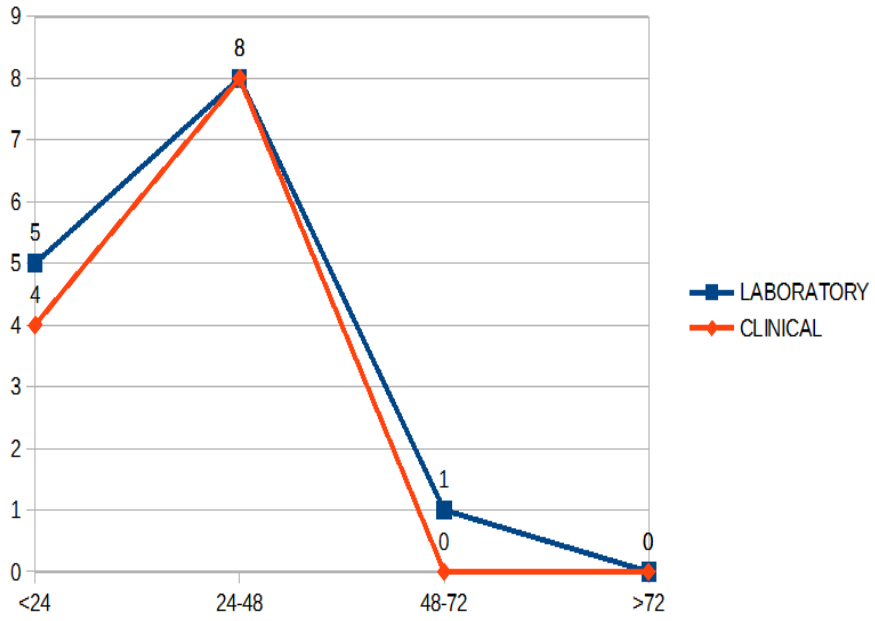


Table 11: Age wise distribution of patients

Age	No. Of Patients (%)	Temporary (%)	Permanent (%)	P – Value
<50 Yrs	39 (78%)	6 (50%)	1 (50%)	0.2999
>50 Yrs	11 (22%)	6 (50%)	1 (50%)	
Total	50 (100%)	12 (100%)	2 (100%)	

Figure 11: Age wise distribution of patients

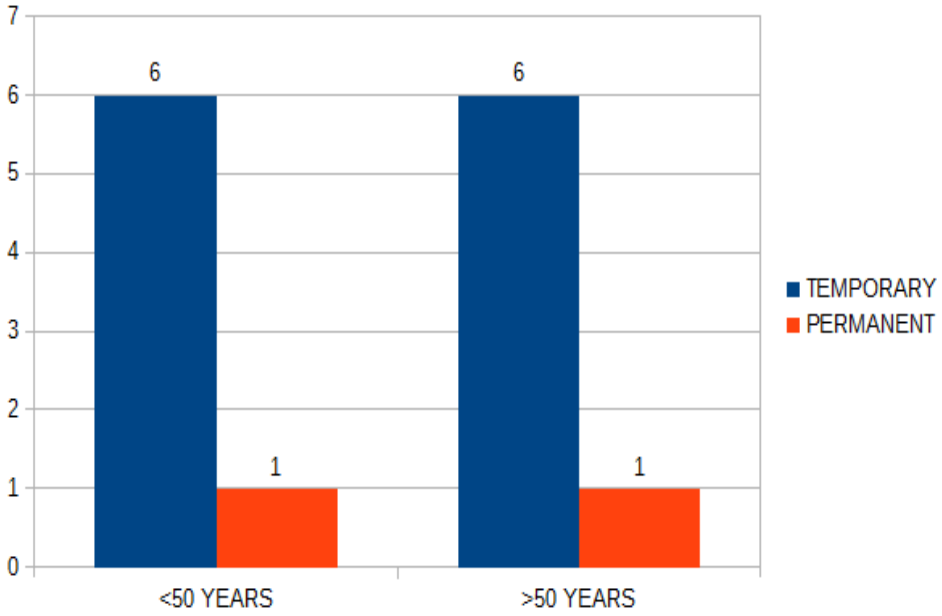


Table 12: Sex wise distribution of hypocalcemia

Sex	No. Of Patients (%)	Temporary (%)	Permanent (%)	P – Value
Male	8 (16%)	2 (16.6%)	0 (0%)	0.82
Female	42 (84%)	10 (83.4%)	2 (100%)	
Total	50 (100%)	12 (100%)	2 (100%)	

Figure 12: Sex wise distribution of hypocalcemia

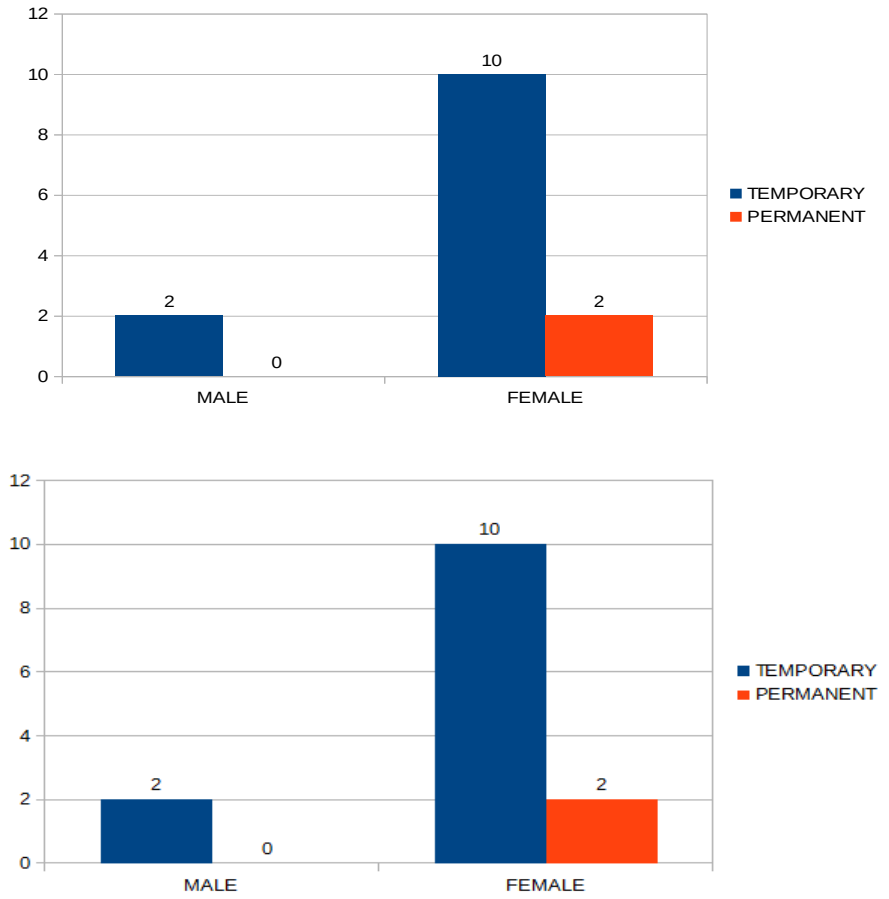


Table 13: Age and sex wise distribution of hypocalcemia

Age	Sex	No. Of Patients (%)	Temporary (%)	Permanent (%)
<50 Years	Male	4 (7.6)	0	0
	Female	35 (78)	8 (66.7)	1 (50)
>50 Years	Male	4 (8)	2 (16.7)	0
	Female	7 (14)	2 (16.7)	1 (50)
Total		50 (100)	12 (100)	2 (100)

Figure 13: Age and sex wise distribution of hypocalcemia

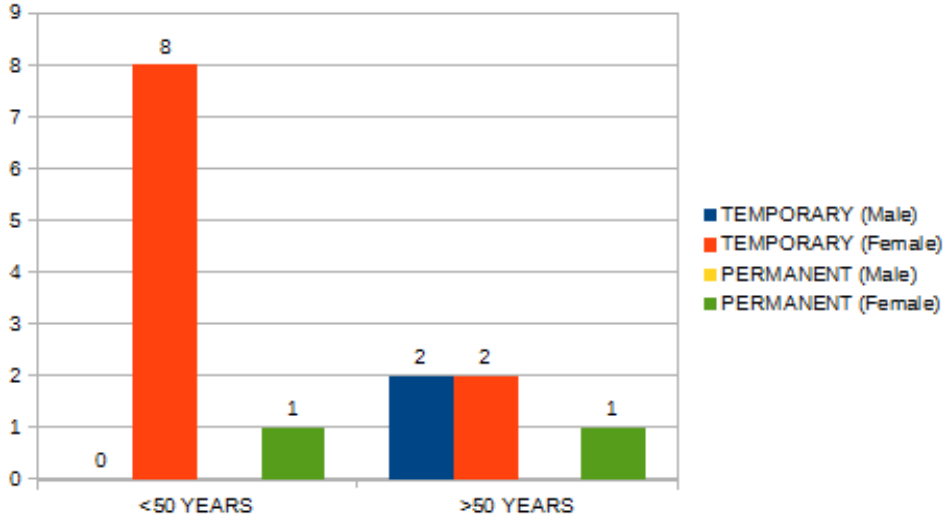


Table 14: Clinical diagnosis wise distribution of hypocalcemia

Clinical Diagnosis	No. Of Patients (%)	Temporary (%)	Permanent (%)	P – Value
Carcinoma	11 (22)	7 (58.3)	0	0.0008
Benign	39 (78)	5 (41.7)	2 (100)	
Total	50 (100)	12 (100)	2 (100)	

Figure 14: Clinical diagnosis wise distribution of hypocalcemia

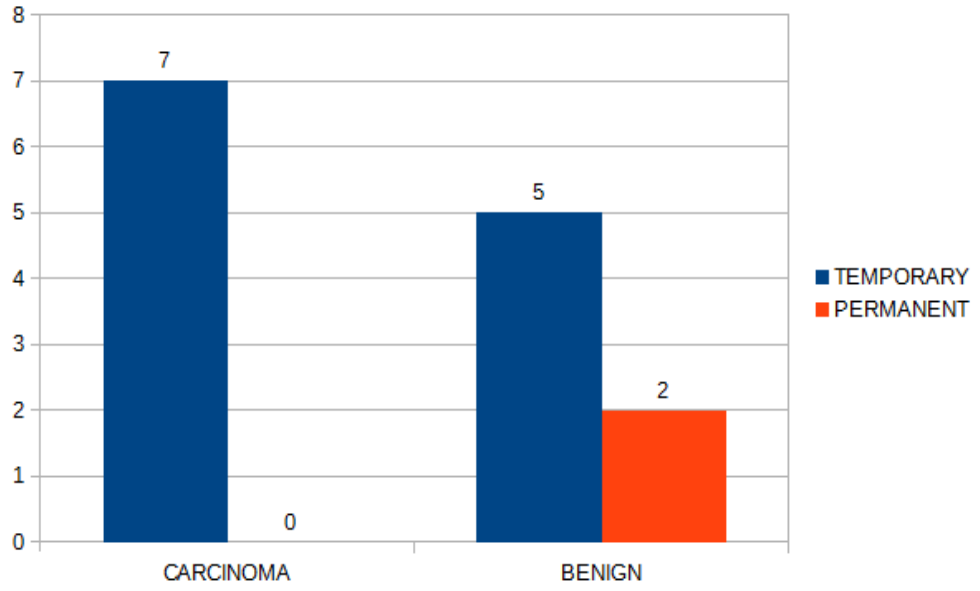


Table 15: Surgery wise distribution of hypocalcemia

Type Of Surgery	No. Of Patients (%)	Temporary (%)	Permanent (%)	P – Value
Total Thyroidectomy	15 (30)	4 (33.3)	2 (100)	0.0293
Near Total Thyroidectomy	10 (20)	5 (41.6)	0	
Sub Total Thyroidectomy	4 (8)	0	0	
Hemi Thyroidectomy	16 (32)	0	0	
Completion Thyroidectomy	5 (10)	3 (25)	0	
Total	50 (100)	12 (100)	2 (100)	

Figure 15: Surgery wise distribution of hypocalcemia

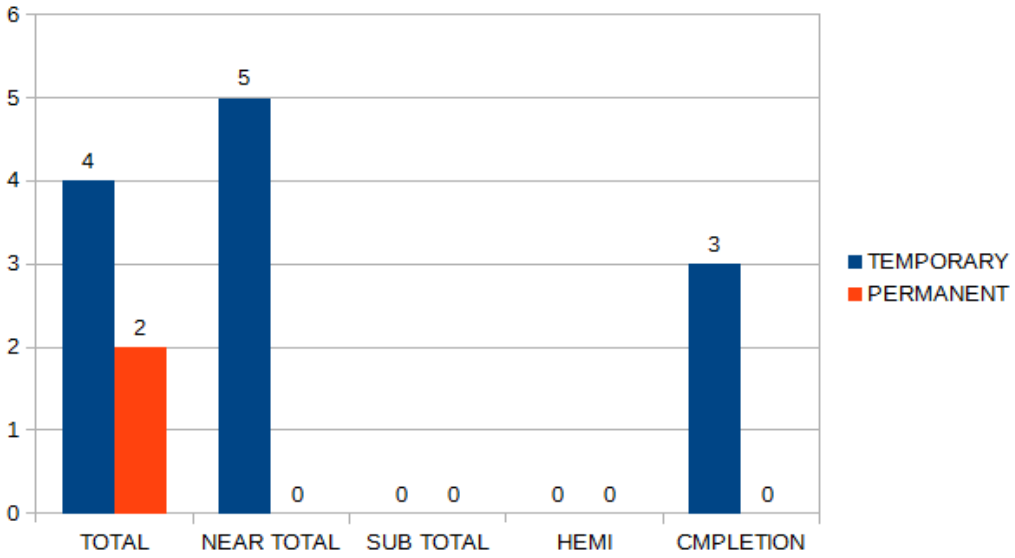


Table 16: Hypocalcemia based on identification of PTG

Identification Of Ptg	Total (%)	Temporary (%)	Permanent (%)	P – Value
Yes	41 (82%)	9 (75%)	1 (50%)	0.3332
No	9 (18%)	3 (25%)	1 (50%)	
Total	50 (100%)	12 (100%)	2 (100%)	

Figure 16: Hypocalcemia based on identification of PTG

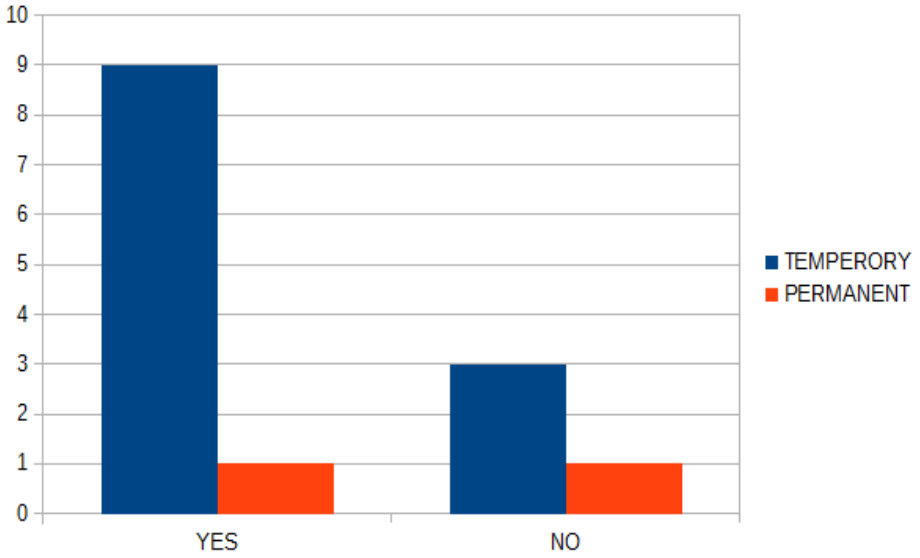


Table 17: Hypocalcemia based on identification of RLN

Identification Of Rln	Total (%)	Temporary (%)	Permanent (%)	P – Value
Yes	35 (70%)	10 (83.3%)	2 (100%)	0.6369
No	15 (30%)	2 (16.7%)	0 (0%)	
Total	50 (100%)	12 (100%)	2 (100%)	

Figure 17: Hypocalcemia based on identification of RLN

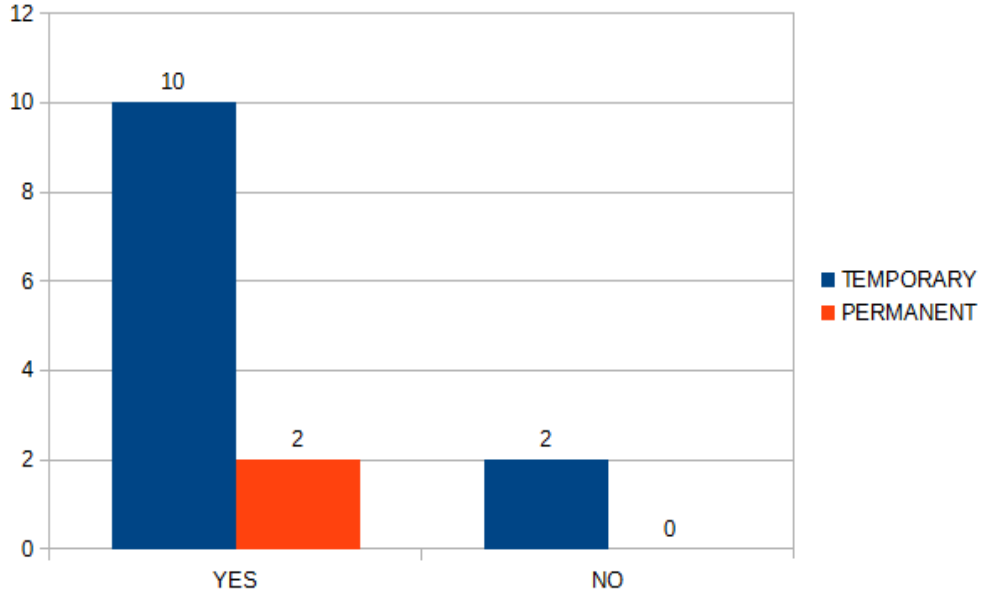
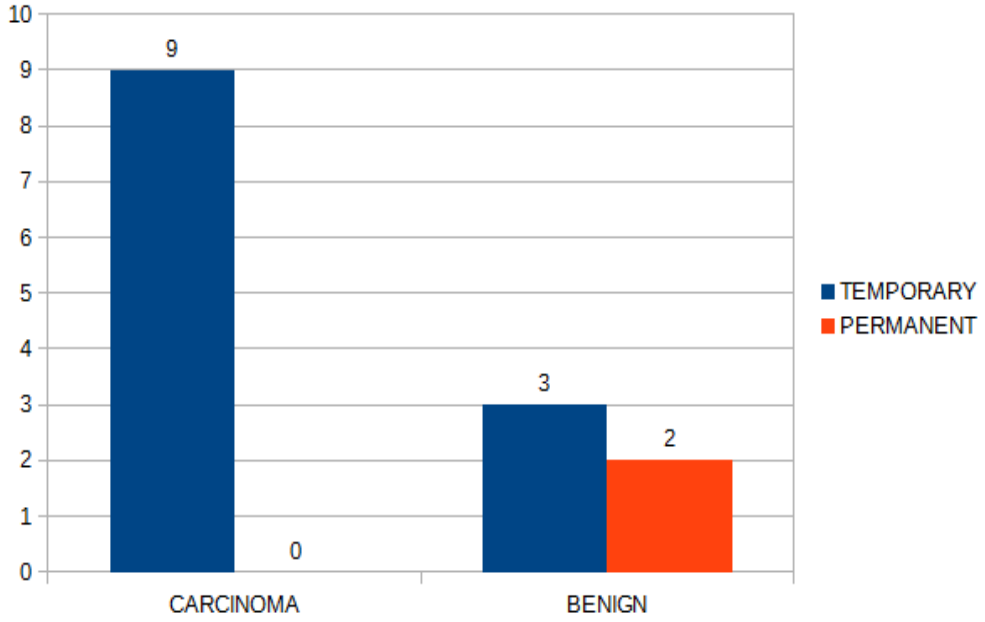


Table 18: Histopathology wise distribution of hypocalcemia

Histopathology	Total (%)	Temporary (%)	Permanent (%)	P – Value
Carcinoma	19 (38%)	9 (75%)	0 (0%)	0.6369
Benign	31 (62%)	3 (25%)	2 (100%)	
Total	50 (100%)	12 (100%)	2 (100%)	

Figure 18: Histopathology wise distribution of hypocalcemia



IX. Discussion

Various thyroid operations are being performed for both benign and malignant disorders of the thyroid. The number of near-total and total thyroidectomies have increased recently. Hypocalcaemia is the most common complication following thyroid surgery and it can be either temporary or permanent. In literature, the definition of permanent hypocalcaemia differs from study to study. Hypocalcaemia is defined as decrease in the serum calcium levels less than the normal with one or more symptom. It is permanent when the patient depends on calcium supplements to maintain a normal calcium level. The period varies from 3 months to 1 year between studies. In our study permanent hypocalcaemia was defined as persistence of laboratory or symptomatic hypocalcaemia beyond three months.Statistical analysis revealed almost 42 million people in India are suffering from thyroid disorders[1]. Women in the age group of 40-60 yrs had highest incidence of thyroid dysfunction.Our institutional analysis showed 104 cases of various thyroid disorders attending the surgical OPD in a year. 62 cases (59.7%) presented with a palpable swelling in the neck. 19(18.3%) cases were referred from other departments within the hospital. 13 (12.5%) cases presented with symptoms of hyper or hypothyroidism. The number of female patients attending the OPD was comparatively high, 76 cases (73%). A total of 53 cases were operated during the study period of which 2 cases were excluded due to low pre-operative calcium values and one case was lost during follow-up.Post-operative hypocalcaemia (temporary or permanent) is the commonest post-operative complication folloing thyroid surgery. The overall prevalence of post-operative hypocalcaemia in our study was 14 patients (28%) temporary hypocalcaemia in 12 patients (24%) and permanent hypocalcaemia in 2 patients (4%) which is consistent with the literature. Of the 14 patients who developed hypocalcaemia, only 12 patients developed signs and symptoms of hypocalcaemia in the post-operative period. The appearance of clinical features of hypocalcaemia occurred typically during the 6 to 48 hour period post-operatively. Symptoms improved following calcium supplementation, by post-operative day 5-7 in all 12 patients who developed transient hypocalcaemia. Of the 2 patients who developed permanent hypocalcaemia, laboratory values remained below normal beyond 6 months during the follow-up period.

Review of literature showed a prevalence of temporary hypocalcaemia ranging from 1.6-23% and permanent hypocalcaemia 0.77-4.2%. Studies by Nair et al on 806 patients showed that the appearance of hypocalcaemia was predominantly during POD 1 and 2. Only 13 patients developed hypocalcaemia during 3rd post-operative day[4]. Sanjana et al observed that patients with an earlier the onset of hypocalcaemia had a high risk of progressing to permanent hypocalcemia[5]. Calo et al related hypocalcaemia as the commonest cause for an extended hospital stay[6]. Studies by Alexandre et al[7], Sperlongano et al [8]and Maralcan et al [9]also showed similar results though ionised calcium was used to monitor the patients. Another observation made by Sturniolo et al was that patients with retrosternal goitre had more acute symptoms (<5 hours)[10]. In our study there were no cases of thyroid disease with retrosternal extension. Tolone et al studied 200 patients in whom 36 patients (18%) had low serum calcium levels. Only 19 of the 36 patients developed symptomatic hypocalcemia[11]. In a study by Kim JH et al 62 of 112 patients developed hypocalcaemia. 9 patients developed only symptoms and 8 had only laboratory hypocalcaemia[12].Due to cost restrictions and limited availability of auto-analysers, ionised calcium was monitored only in restricted number of patients in our study. Serum calcium measured during the post-

operative period (6th, 24 and 48 hours) was cost-effective and sensitive for detection and treatment of post-operative hypocalcaemia.

Studies by Del Rio et al compared the measurements of ionised calcium and serum calcium in a series of 492 cases of thyroidectomy. In their study they concluded that ionised calcium was only a diagnostic aid, but not an effective marker of hypocalcemia[13]. A calcium slope was created based on the post-operative measurements of serum calcium at various intervals in a study by Walsh et al. In their study 19 of 52 patients developed hypocalcaemia on day 1 of surgery which was effectively predicted by serum calcium measurement at 6th hour post- operatively[14]. Miccoli et al[16] and Lombardi et al [15]made an observation on the early measurements of iPTH post-operatively and found that it had a low accuracy rate in prediction of post-operative hypocalcaemia. Asari et al found that the combined measurement of iPTH and serum calcium carried a high positive predictive value when compared to either of it measured alone[17].In our study a female predominance (84%) was observed. The female to male ratio was 5.25:1. In our study the sex of the patient did not influence the outcome of post-operative hypocalcaemia. This observation has been made in studies by Nair et al[4], Qasaimeh et al[18] and cannon et al. This is in contradiction to studies made by Del rio et al[19] and Edafe et al[20] in which female gender had a statistically significant role in the post-operative outcome of hypocalcaemia.

In our study thirty nine (78%) patients fell in the age group of less than 50 years with a mean age of 39.08 years. Chi-Square test failed to show a statistical significance for age of the patient to affect the prevalence of post-operative hypocalcaemia. Pfleiderer et al [21]and Gopalakrishnan Nair et al [4]observed the same in their clinical study. Studies by Bhattacharya et al showed a higher incidence of hypocalcaemia in younger patients. Whereas a study by Alexandre et al on 333 patients showed that patients above 50 years had 1.9 times higher chances of developing hypocalcaemia[22] . Study by Tolone et al showed a 20 fold increase in risk of post-operative hypocalcaemia in elderly patients (>50yrs)[11].In our study there were 45 cases of primary surgery and 5 cases of completion thyroidectomy. The order of frequency of operations performed was Hemi>Total>Near total>Sub-total. Hypocalcaemia occurred in the group of patients undergoing near total and total thyroidectomies. There were no incidence of hypocalcaemia in patients undergoing hemi and sub-total thyroidectomy. 4 out of 5 cases undergoing re-surgery developed post-operative hypocalcaemia, though it was temporary. The two patients who developed permanent hypocalcaemia had undergone total thyroidectomy for a benign disease. In our study the extent of surgery showed a statistical significance with regards to post-operative hypocalcaemia.Studies by Bergamaschi et al[23] and De Falco et al[24] showed a similar outcome. The rates of hypocalcaemia were significant in the group of patients undergoing total thyroidectomies. The outcome of a study by Meyer et al[25] supported this view. Also in his study he observed a higher rate of complications in patients undergoing re-operation. Studies by De Pasquie et al[26], Bhattacharya et al[27] and Walsh et al [14]failed to show a statistical significance of type of surgery on the prevalence of post-operative hypocalcaemia.

Attempts were made to identify and preserve parathyroid and RLN in all 50 patients undergoing thyroidectomy. All four parathyroid glands were identified only in two patients. RLN was identified either unilaterally or bilaterally in 35 patients (70%) undergoing various thyroidectomies. Patients were grouped into two based on the identification of RLN, Parathyroid glands. There was no statistical significance as observed in post-operative hypocalcaemia based on the identification of parathyroid or RLN in our study. Only one patient underwent parathyroid re-implantation following inadvertent removal, which was not significant to make a comparative study.Hakan et al studied 134 thyroidectomies and grouped patients into two based on identification of RLN. They observed that with regards to hypocalcaemia there was no significant difference was found between the two groups[29]. However, in a similar study by Megherbi et al the dissection to identify RLN was a risk factor for post-operative hypocalcaemia[28].Studies by Walsh et al[14], Gourgiotis et al[30] and Lin et al[31] showed that the intra-operative parathyroid identification, inadvertent removal of parathyroid and parathyroid re-implantation did not seem to affect the post-operative outcome of hypocalcaemia. Contradictory to this finding Meyer et al[25] and Qasaimeh et al[32] observed that intra-operative parathyroid identification and re-implantation had a statistical significance based on the post-operative outcome of hypocalcaemia.Of the 50 patients who underwent thyroidectomies a clinical diagnosis of carcinoma thyroid was suspected in 11 patients (22%) and the rest of 39 patients (78%) were diagnosed with a benign disorder. Based on the histopathology report there were 19 patients (38%) with the diagnosis of malignancy and 31 patients (62%) were found to have benign pathology. The prevalence of temporary hypocalcaemia was more in patients with carcinoma of thyroid, whereas the two patients developed permanent hypocalcaemia had a benign pathology.Transient hypocalcaemia developed in nine out of 19 patients(38%) diagnosed to have carcinoma of thyroid based on histopathology. Transient hypocalcaemia developed in three out of thirty one patients (62%) with benign thyroid pathology. The final histopathology reports of the two patients who developed permanent hypocalcaemia showed evidence of multi-nodular goitre. Both these patients were females within the age group of 40-60 years. Statistical analysis showed an overall significance with regards to clinical diagnosis and histopathology.

Edafe et al [20]and Nair et al[4] observed that patients undergoing thyroidectomy for toxic goitres had a higher incidence of hypocalcaemia probably due to high vascularity leading to increased use of cautery and

subsequent ischaemic damage to parathyroid. Del Rio et al observed a significant post-operative hypocalcaemia for patients undergoing surgery for malignancy[19]. Findings were supported in the study by Sciume et al that the histopathology of the gland played a significant role in post-operative hypocalcaemia[33]. Alexandre et al compared symptoms of hypocalcaemia within various groups based on histopathology[22]. Colloid goitres had the lowest rates of temporary and permanent hypocalcaemia. Interestingly in a recent trial by Nair et al showed that auto-immune thyroid disorders played a vital role in post-operative outcome of hypocalcaemia. The rate of permanent hypocalcaemia was statistically significant in the 6 patients diagnosed with classical Hashimoto[4].It is important to identify the possible risk factors and predictors of post- thyoidectomy hypocalcaemia. Early measurements of serum calcium can be a life saving measure and prevent devastating complications of the surgery. Meticulous capsular dissection is essential to prevent inadvertent removal or injury to the parathyroid glands. At-least 2 parathyroid glands should be preserved to maintain normocalcaemia. Post-operative hypocalcaemia is a multi-factorial phenomenon and no single factor can accurately predict the outcome of the surgery. Though studies have showed that parathyroid transplant protects against developing permanent hypocalcaemia, routine transplant should be avoided[34]. Further studies regarding the usefulness of parathyroid re-implantation are required to arrive at a logistical analysis. A general consensus should be arrived on the definition of permanent and temporary hypocalcaemia since the time duration varies within several studies from 1 month to 1 year. The ultimate aim of the operating surgeon should be to prevent complications than predicting it. Routine monitoring of serum total or ionized calcium and timely intervention can prevent the life threatening complications of hypocalcaemia.

X. Limtations Of The Study

1. Small sample size, although 50 patients were recruited, when divided into groups based on type of surgery, histopathology, the numbers were relatively small in each group.
2. Due to cost restrictions and limited availability of auto analysers the ionized calcium and parathormone levels were not recorded, which could have yielded a better result.
3. Follow up period was also limited.

XI. Summary &Conclusion

This study "The prevalence and outcome of post-thyroidectomy hypocalcaemia" a prospective observational study conducted at Tertiary care teaching hospital from February 2014 to April 2015. In our study a total of 50 patients undergoing various thyroid operations were followed for post-thyroidectomy hypocalcaemia over a period of three months.The prevalence of hypocalcaemia observed in our study was 14 patients (28%). Temporary hypocalcaemia was seen in 12 patients (24%) and permanent hypocalcaemia in 2 patients (4%).The prevalence of temporary hypocalcaemia was predominantly noted in the patients undergoing surgery for carcinoma of thyroid. Univariate analysis of clinical diagnosis and histopathology on the outcome of hypocalcaemia produced statistically significant results.The extent of thyroid resection plays a vital role in the outcome of post-thyroidectomy hypocalcaemia. Results were statistically significant for total thyroidectomy on the outcome of hypocalcaemiaPatient related factors like age and gender did not influence the outcome of post-thyroidectomy hypocalcaemia. Results were statistically insignificant for age and sex of patient.Identification and preservation of the parathyroid, RLN did not protect against hypocalcaemia. Results in our study for identification of RLN and PTG respectively were statistically insignificant and did not influence the outcome of post-operative hypocalcaemia.In 13 patients the onset of hypocalcaemia was within 48hours post-operatively. Only 12 out of 14 patients developed symptoms of hypocalcaemia.Based on the observations made in our study we conclude that the clinical diagnosis, histopathology and type of thyroid surgery were significant risk factors for development of post-operative hypocalcaemia. Age, Gender, Identification of RLN or Parathyroid gland did not influence the outcome of post-thyroidectomy hypocalcaemia.Limited number of patients was an important drawback of the study. Measurement of parathormone and ionised calcium would have yielded a more sensitive result. These were not done due to cost restrictions and limited availability.

References

[1]. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011 Jul; 15(Suppl 2): s78-81.
[2]. Agarwal GS, MK Singh M. The prevalence of thyroid dysfunction among South Indian women with Metabolic Syndrome. J Clin Diagn Res. 2011; 5(2)(2): 213-6.
[3]. Urbano, FL. Signs of hypocalcemia: Chvostek's and Trousseau's signs. Hosp Physician. 2000 Mar; 43-45.
[4]. C.Gopakrishnan Nair, Mishra J.C.Babu, Rijju menon, Pradeep Jacob Hypocalcemia following total thyroidectomy. Indian J Endocrinol Metab. 2013 Mar-Apr; 17(2): 298-303.
[5]. Nemade SV, Chirmade AP. Post-thyroidectomy early serum ionic calcium level: Predictor of prolonged hypocalcemia. Ear Nose Throat J. 2013 Aug;92(8):382- 90.
[6]. Khanzada TW, Samad A, Memon W, Kumar B. Post thyroidectomy complications: the Hyderabad experience. J Ayub Med Coll Abbottabad JAMC. 2010 Mar; 22(1): 65-8.

[7]. Prichard RS, Edhouse PJ, Sidhu SB, Sywak MS, Delbridge L. Post-operative partial hypoparathyroidism: an under-recognized disorder. ANZ J Surg. 2011 Aug; 81(7-8): 524-7.
[8]. Sperlongano P, Sperlongano S, Foroni F, De Lcia FP, Pezzulo C, Manfredi C et al. Postoperative hypocalcemia: Assessment timing. Int J Surg Lond Engl. 2014 May 22.
[9]. Maraclan G, Sayin Z, Baskonu I, Gokalp A, Aybasti N. Does truncal ligation of the inferior thyroid arteries during bilateral subtotal thyroidectomy affect serum calcium levels? A prospective, randomized, controlled study. Int Surg. 2006 Aug; 91(4): 211-6.
[10]. Sturniolo G, Lo Schiavo MG, Tonante A, D'Alia C, Bonanno L. Hypocalcemia and hypoparathyroidism after total thyroidectomy: a clinical biological study and surgical considerations. Int J Surg Investig. 2000; 2(2): 99-105.
[11]. Tolone S, Roberto R, del Genio G, Brusciano L, Parmeggiani D, Amoroso V, et al. The impact of age and oral calcium and vitamin D supplements on postoperative hypocalcemia after total thyroidectomy. A prospective study. BMC surg. 2013;13 suppl 2:S11.
[12]. Kim JH, Chung MK, Son Y-I. Reliable early prediction for different types of post thyroidectomy hypocalcemia. Clin Exp Otorhinolaryngol 2011 Jun; 4(2): 95-100.
[13]. Del Rio P, Arcuri MF, Cataldo S, Palladino S, Sianesi M. Can we use ionized calcium in the evaluation of post-thyroidectomy hypocalcemia? Minerva Endocrinol. 2009 Dec; 34(4): 289-93.
[14]. Gourgiotis S, Moustafellos P, Dimopoulos N, Papaxoinis G, Baratsis S, Hadjiyannakis E. Inadvertent parathyroidectomy during thyroid surgery: the incidence of a complication of thyroidectomy. Langenbecks Arch Surg Dtsch Ges Für Chir. 2006 Nov; 391(6): 557-60.
[15]. Lombardi CP, Raffaelli M, Princi P, Dobrinja C, Carrozza C, Di Stasio E, et al. Parathyroid hormone levels 4 hours after surgery do not accurately predict post-thyroidectomy hypocalcemia. Surgery. 2006 Dec; 140(6): 1016-1023; discussion 1023-1025.
[16]. Miccoli P, Minto MN, Panicucci E, Cetani F, D'Agostino J, Vignali E, et al. The impact of thyroidectomy on parathyroid glands: a biochemical and clinical profile. J Endocrinol Invest. 2007 Sep; 30(8): 666-71.
[17]. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. Arch Surg Chic III 1960. 2008 Feb; 143(2): 132-137; discussion 138.
[18]. Cannon CR, Replogle WH. Hypocalcemia following hemithyroidectomy. J Miss state Med Assoc. 2008 Sep; 49(9): 265-9.
[19]. Del Rio P, lapichino G, De Simone B, Bezer L, Arcuri M, Sianesi M. Is it Possible to identify a risk factor condition of hypocalcemia in patients candidates to thyroidectomy for benign disease? Ann Ital Chir. 2010 Dec;81 (6):397-401.
[20]. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian sp. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. Br J Surg. 2014 Mar; 101(4): 307-20.
[21]. Pfleiderer AG, Ahmad N, Draper MR, Vrotsou K, Smith WK. The timing of calcium measurements in helping to predict temporary and permanent hypocalcaemia in patients having completion and total thyroidectomies. Ann R coll surg Engl. 2009 Mar; 91(2): 140-6.
[22]. Sousa A de A, Salles JMP, Soares JMA, Moraes GM de, Carvalho JR, Savassi-Rocha PR. Predictors factors for post-thyroidectomy hypocalcaemia. Rev Colégio Bras Cir. 2012 Dec; 39(6): 476-82
[23]. Meyer T, Merkel S, Radespiel-Troeger M, Hohenberger W. [Dysfunction of calcium metabolism following resection of the thyroid gland. An analysis of important risk factors]. Zentralblatt Fur Chir. 2002 May; 127(5): 429-34.
[24]. Sciume C, Geraci G, Pisello F, Facella T, Li Volsi F, Licata A, et al. [Complications in thyroid surgery: symptomatic post-operative hypoparathyroidism incidence, surgical technique, and treatment]. Ann Ital Chir. 2006 Apr; 77(2): 115-22
[25]. Vaiman M, Nagibin A, Olevson J. Complications in primary and completed thyroidectomy. Surg Today. 2010; 40(2): 114-118.
[26]. De Falco M, Parmeggiani D, Giudicianni C, Lanna A, Miranda A, Oliva G, et al. [Post-thyroidectomy hypocalcemia. Personal experience]. Minerva Endocrinol 2002 Sep; 27(3)
[27]. De Pasquale L, Schubert L, Bastagli A. Post-thyroidectomy hypocalcemia and feasibility of short-stay thyroid surgery. Chir Ital. 2000 Oct; 52(5): 549-54.
[28]. Megherbi MT, Graba A, Abid L, Oulmane D, saidani M, Benabadji R. [Complications and sequelae of benign thyroid surgery]. J Chir (Paris). 1992 Jan; 129(1): 41-6.
[29]. Canbaz H, Dirlik M, Colak T, Ocal K, Akca T, Bilgin O, et al. Total thyroidectomy is safer with identification of recurrent laryngeal nerve. J Zhejiang Univ Sci B. 2008 Jun; 9(6): 482-8.
[30]. Bergamaschi R, Becouarn G, Ronceray J, Arnaud JP. Morbidity of thyroid surgery. Am J Surg. 1998 Jul; 176(1): 71-5.
[31]. Lin DT, Patel SG, Shaha AR, Singh B, Shah JP. Incidence of inadvertent parathyroid removal during thyroidectomy. The Laryngoscope. 2002 Apr; 112(4): 608-11.
[32]. Qasaimeh GR, A1 Nemri S, A1 Omari AK. Incidental extirpation of the parathyroid glands at thyroid surgery: risk factors and post-operative hypocalcemia. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino- Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2011 Jul; 268(7): 1047-51.
[33]. Walsh SR, Kumar B, Coveney EC. Serum calcium slope predicts hypocalcaemia following thyroid surgery. Int J Surg Lond Engl. 2007 Feb;5(1):41-4.
[34]. Trupka A, Sienel W. [Autotransplantation of at least one parathyroid gland during thyroidectomy in benign thyroid disease minimizes the risk of permanent hypoparathyroidism]. Zentralblatt Fur Chir. 2002 May; 127(5): 439-42.