Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/cameav89

CLINICAL EVALUATION OF HYPOCALCEMIA AFTER THYROIDECTOMY

Dr. Hemand N M[1*], Dr. Amisha Saxena[2], Dr. Nishitha Prashanth[3], Dr. Tripti Pandey[4]

[1*]MBBS MS, General Surgery, Rajarajeswari Medical College, Bangalore, India
natarajanhemand@gmail.com
[2]MBBS MS, General Surgery, Rajarajeswari Medical College, Bangalore, India
[3]MBBS MS, General Surgery, Rajarajeswari Medical College, Bangalore, India
[4]MBBS MS, General Surgery, Rajarajeswari Medical College, Bangalore, India

STRUCTURED ABSTRACT

Background and objectives: To estimate the incidence of hypocalcemia after total thyroidectomy also in relation with various pathological thyroid conditions and timing of presentation of hypocalcemia.

The aim of the study was to estimate the incidence of hypocalcemia after total thyroidectomy as post thyroidectomy hypocalcemia is a common complication and if not timely untreated or follow up leading to serious conditions to patients.

Methods: The Prospective observational study was done in patients who admitted in General surgery ward of our department for various Thyroid pathological conditions with 49 patients undergoing total thyroidectomy. A proforma will be used to collect information and estimate the incidence of post total thyroidectomy hypocalcemia with serial monitoring of serum calcium, with observation of signs and symptoms of hypocalcemia.

Result and Discussion: In this study, 49 patients were included. From the present study the incidence of hypocalcemia is 32.6%. Thyroid diseases are found more common in female 87.8%, with post thyroidectomy hypocalcemia seeing more in older age group 62% in (45-60) years comparing to younger age group. In relation to pre op indications of thyroidectomy with outcomes of hypocalcemia our study shows increased incidence of hypocalcemia in malignancy 57% of 100% and Grave's disease 50% out of 100%, MNG 26% out of 100% . Parathyroid gland is the most significant factor for post thyroidectomy hypocalcemia so careful identification, preservation is important and if devascularized or injured to gland autotransplantation of gland should be done.

Conclusion: The incidence of hypocalcemia is 32.6% in my study with more incidence found in older age, malignant lesion, Grave's disease, female sex. x Parathyroid glands identification and preservation plays key role in post thyroidectomy hypocalcemia.

Keywords: Parathyroid, serum calcium, thyroid gland, autotransplantation, proper anatomical knowledge.

INTRODUCTION

Thyroid disorders are the second most common endocrinological disorder following diabetes. In India estimated population of 42 million are said to be suffering from thyroid disorders. The thyroid gland is a centrally located structure in the anterior neck. As an endocrine organ, it plays a crucial role in producing thyroid hormones and calcitonin, which are vital for regulating metabolism, growth, and serum electrolyte levels, particularly calcium.

The thyroid gland can be affected by various conditions, with disruptions in hormone production leading to hypothyroidism or hyperthyroidism. It is also implicated in inflammatory disorders (such as thyroiditis), autoimmune diseases (like Graves' disease), and cancers (including papillary thyroid carcinoma, medullary thyroid carcinoma, and follicular carcinoma).
Beyond its functions in metabolism, growth, and electrolyte regulation, the thyroid's anatomical position is important, as it is closely associated with critical structures such as the parathyroid glands, recurrent laryngeal nerves, and various blood vessels. [1,6]

Thyroid disorders can be addressed through either medical or surgical treatments. One of the most commonly performed surgeries globally is thyroidectomy. Indications for this procedure include symptoms of compression, suspected or confirmed malignancy, the presence of a solitary cold nodule in individuals under 20 years old, cosmetic concerns, and the existence of a complex cyst or a cyst larger than 4 cm. Thanks to advancements in anesthesia, surgical techniques, antiseptic practices, improved instruments, and a better understanding of thyroid anatomy and physiology, thyroid surgery is now regarded as a safe procedure. Nonetheless, complications can still arise following thyroid surgery, including hypocalcemia, injury to the recurrent laryngeal nerve, hematoma, seroma, stridor, loss of high-pitched voice, injury to the thoracic duct, wound infection, and damage to the trachea. These complications tend to occur less frequently when the surgery is performed by experienced surgeons. Among these, hypocalcemia and recurrent laryngeal nerve injury are the most commonly observed. Postoperative complications may be influenced by several risk factors, including age, gender, gland size, type of thyroid disease, presence of fibrosis and inflammation, extent of the thyroidectomy, and lymph node dissection.[2]

Post-thyroidectomy hypocalcemia typically results from the removal, devascularization, or damage to the parathyroid glands, leading to either transient or permanent hypoparathyroidism. Other contributing factors may include vitamin D deficiency, a sudden rise in serum calcitonin levels, or a condition known as "hungry bone syndrome." Additionally, postoperative alkalosis-induced hypocalcemia, caused by hyperventilation due to postoperative pain, and dilutional hypocalcemia are also considered potential causes.

Although the rate of hypocalcemia has decreased with the advancement of parathyroid-preserving techniques, transient hypocalcemia still occurs in 6.9% to 49.0% of patients who undergo thyroidectomy. A surgeon's ability to predict the onset of post-thyroidectomy hypocalcemia plays a crucial role in post-operative care. Early identification of patients at risk can shorten hospital stays and eliminate the need for unnecessary laboratory tests. If hypocalcemia is anticipated, the use of prophylactic calcium and vitamin D supplementation can help prevent symptoms of hypocalcemia and allow for earlier discharge. Numerous studies have attempted to identify risk factors for early hypocalcemia after thyroid surgery, with varying results. Postoperative hypoparathyroidism remains a significant challenge for thyroid surgeons due to its prevalence and the limited understanding of its relationship with early hypocalcemia development.[3]

Although thyroidectomy is generally considered a safe procedure, post- thyroidectomy hypocalcemia is a common complication. In most cases, this hypocalcemia is transient, but it can become permanent if there is a loss of functioning parathyroid glands, leading to significant discomfort for affected patients, who may need to take oral calcium and vitamin D supplements long-term. Potential causes of hypocalcemia include injury to the parathyroid glands or their blood supply, extensive resection, neck dissection with total thyroidectomy, Graves' disease, carcinoma, and hemodilution. Among these, parathyroid gland injury is the most frequent cause of hypocalcemia. To minimize the risk of parathyroid injury, surgeons should make an effort to locate and preserve all the parathyroid glands and their blood supply. However, it can be challenging to identify and protect these glands due to the high risk of damaging their blood supply during dissection. Additionally, the extent of the thyroidectomy and lymph node dissection increases the likelihood of damaging the parathyroid glands' blood supply. Many studies have suggested that parathyroid autotransplantation can reduce the incidence of hypocalcemia, particularly when parathyroid glands are unintentionally removed or devascularized during surgery.[4]

This study aims to explore the incidence and risk factors associated with post-thyroidectomy hypocalcemia.

RATIONALE

After diabetes, thyroid disorders are the second most endocrine disorders. Recent studies in south india shows Thiruvananthapuram ranks the highest thyroid malignancy. Post thyroidectomy hypocalcemia is well recognized complications. This study aims to estimate the occurrence of post thyroidectomy hypocalcemia. It also aims to identify post thyroidectomy hypocalcemia in relations to various pathological conditions, study of timing of presentation of post thyroidectomy hypocalcemia.

RESEARCH QUESTION

What‘s the incidence of hypocalcemia after total Thyroidectomy at Govt.TD Medical College, Alappuzha

OBJECTIVES

PRIMARY OBJECTIVE:

1. To estimate the incidence of hypocalcemia after total Thyroidectomy.

SECONDARY OBJECTIVE:

2. Post thyroidectomy hypocalcemia in relations with various pathological thyroid conditions.
3. To study timing of presentation of post thyroidectomy hypocalcemia.

REVIEW OF LITERATURE

Embryology of the Thyroid Gland

It‘s a midline derivative of pharynx. First identifiable in stage 11-12 embryos as median thickening of endoderm lying in floor of pharynx between first and second pharyngeal pouches and immediately dorsal to aortic sac. The foramen caecum is the site of median diverticulum that appears in furrow immediately caudal to median tongue bud. It extends caudally as thyroglossal duct, passing ventral to primordium of hyoid bone and reaches rostral border of aortic sac by stage 15. The tip of duct bifurcates and tissue mass subsequently divides to form isthmus and lateral lobes of thyroid gland. The endoderm derived epithelial tissue is invested by vagal neural mesenchyme, giving rise to connective tissue capsule, interlobular septa, perifollicular mesenchyme, which carries neurovascular and lymphatic supply to gland [5]

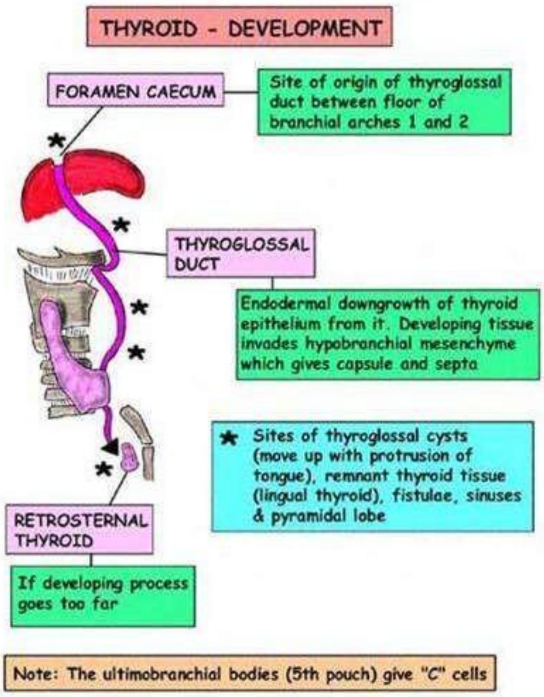


Fig.1-Embryology of Thyroid gland

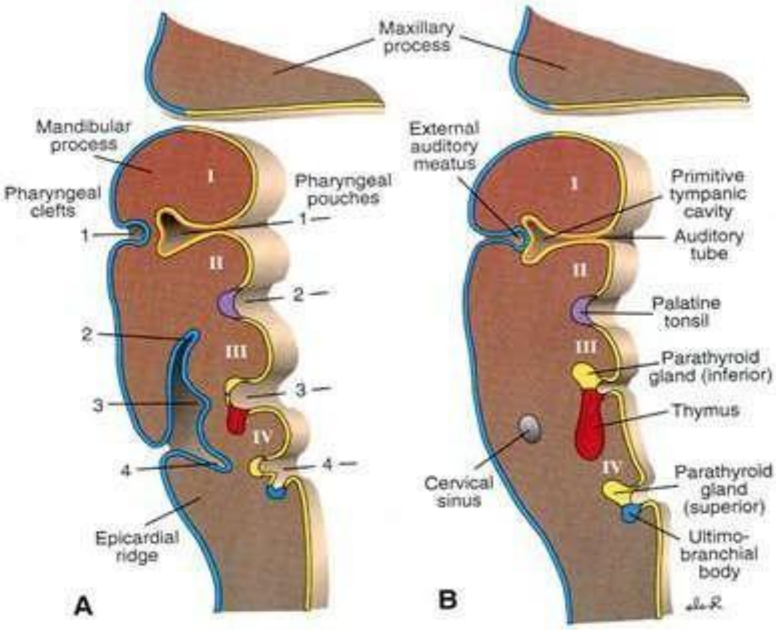


Fig.2-Pharyngeal arch transformation

Thyroid Gland

The thyroid gland is consist of two lobes connected by an isthmus, which crosses the midline of trachea at the level of the second and third tracheal rings. Anatomically, the thyroid lies behind the sternothyroid and sternohyoid muscles, encircling the cricoid cartilage and the tracheal rings. It is positioned below the laryngeal thyroid cartilage, usually spanning the vertebral levels C5 to T1. The thyroid is anchored to the trachea by a dense connective tissue structure known as the lateral suspensory ligament or Berry's ligament, which links each thyroid lobe to the trachea. Together with the esophagus, pharynx, and trachea, the thyroid resides within the neck's visceral compartment, which is surrounded by the pretracheal fascia.

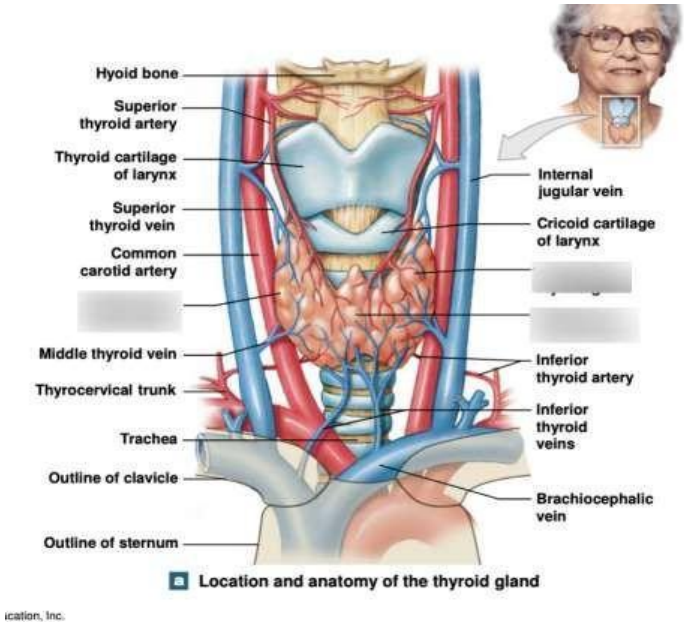


Fig.3-Anatomy of Thyroid gland

In its typical form, the thyroid gland has symmetrical lateral lobes and a clearly defined, centrally located isthmus. The gland often includes a pyramidal extension at the posterior-most part of each lobe, called the tubercle of Zuckerkandl. While these features are common, the thyroid exhibits significant anatomical variations. The location of the thyroid gland and its proximity to other vital structures presents several surgical considerations with important clinical implications. [6]

Pyramidal Lobe

The pyramidal lobe (PL) forms when the distal part of the thyroglossal duct remains, appearing in 44–61% of cases, typically at the upper edge of the isthmus. Pyramidal lobe is a dense fibrous band with little thyroid tissue within a normal thyroid gland. Its clinical importance arises when it is not removed during a total thyroidectomy, potentially leading to:

(a) Hyperthyroidism recurrence due to compensatory growth in toxic goiters
(b) Goiter recurrence in cases of nodular goiters
(c) Recurrence of malignancy in differentiated thyroid cancer caused by multifocality
(d) Recurrent thyroglossal fistula after an incomplete Sistrunk's procedure.

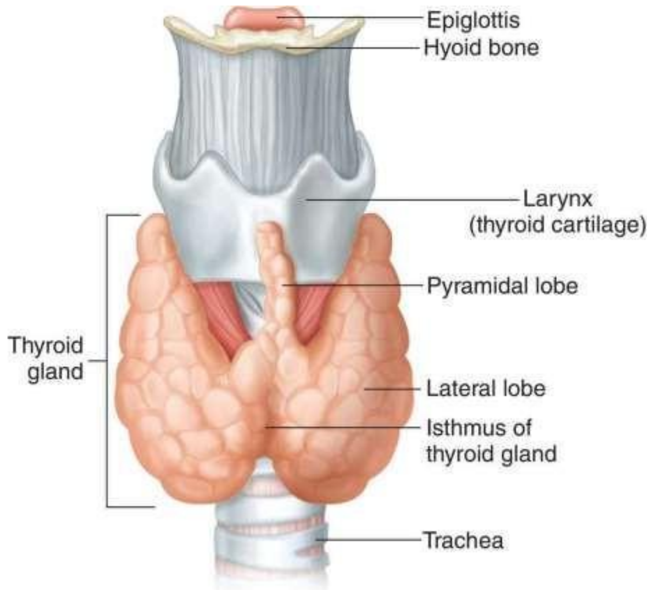


Fig.4-Pyramidal lobe

Ligament of Berry (LB):

The ligament of Berry is formed by the condensation of pretracheal fascia along with a thin layer of thyroid parenchyma that is entrapped on posterolateral aspect of thyroid gland. It serves to suspend and securely attach the thyroid to the cricoid cartilage and the upper tracheal rings. This ligament plays a crucial role in thyroid movement during swallowing. During surgery, excessive medial rotation of the thyroid can lead to kinking of the recurrent laryngeal nerve (RLN) due to its close proximity to the ligament, which causes significant risk of RLN injury during thyroidectomy. Identifying the RLN and performing a careful capsular dissection near the ligament of Berry is essential for ensuring quality thyroid surgery. [7]

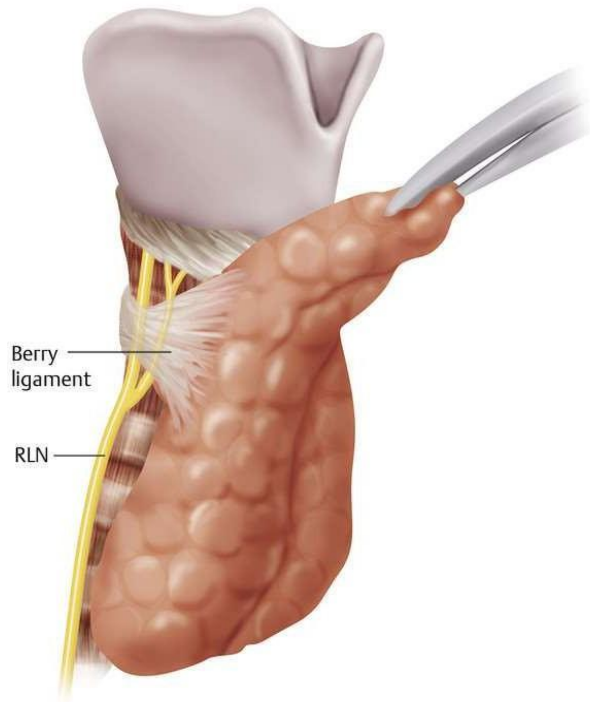


Fig.5-Ligament of Berry and Recurrent laryngeal nerve

Tubercle of Zuckerkandl (TZ):

The tubercle of Zuckerkandl is a localized area of thyroid tissue found at the cricothyroid junction on the posterolateral side of the thyroid gland. Its clinical significance lies in its role as a surgical landmark, particularly in identifying the location of the recurrent laryngeal nerve (RLN). This anatomical feature serves as a reliable reference, as the RLN enters the larynx just behind it, making it a crucial guide during thyroid surgery. [7,8]

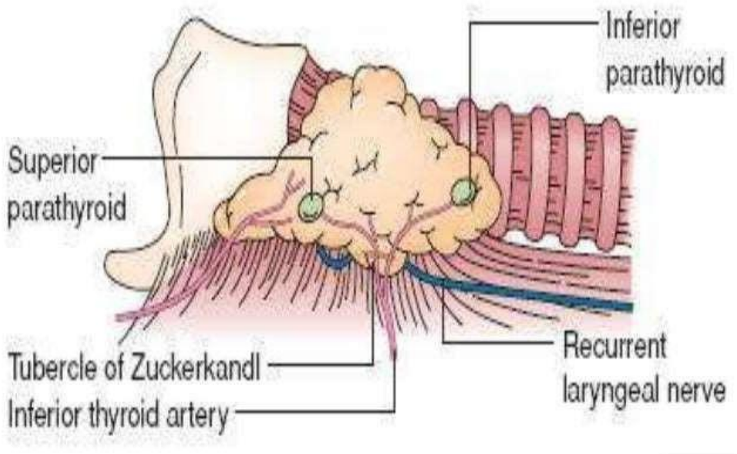


Fig.6-Tubercle of Zuckerkandl Recurrent laryngeal nerve:

The left and right recurrent laryngeal nerves (RLN) are the two key nerves that pass through the thyroid gland. These nerves are typically located on the lateral side of the gland, near the inferior thyroid artery. During thyroid surgery, it is crucial to identify and protect these nerves from injury. The nerve can be accessed beneath the inferior thyroid artery or after mobilizing the superior and inferior poles. The distal part of the nerve, typically the last 2-3 cm, is most vulnerable to damage. This portion is often shielded by the tubercle of Zuckerkandl (a pyramidal projection at the posterior edge of each thyroid lobe) and the ligament of Berry. The RLN is frequently obscured from view, running just medial to the tubercle, and is usually visualized only when the tubercle is retracted. In total lobectomy procedures, the RLN's distal path is more easily identified compared to subtotal lobectomies, where this portion may not be visible.

Surgical planning must also consider anatomical variations of the nerves. In about 1% of cases, a nonrecurrent laryngeal nerve or a direct vagus branch may be seen on the right side after retracting the tubercle of Zuckerkandl.

Additionally, due to variations in the RLN's branching patterns—such as bifurcation or trifurcation near its entrance to the larynx—care must be taken not to cut or clamp any nerve branches within the ligament of Berry.

Finally, nerve injury can result not only from direct trauma but also from thermal damage caused by electrocautery when used near the nerves. [8]

Blood supply:

Artery:

Thyroid gland is supplied by superior and inferior thyroid arteries and sometime by arteria thyroidea ima from brachiocephalic trunk or aortic arch. Arteries are large, their branches anastomose frequently both on and in the gland, ipsilaterally and contralaterally.

The superior thyroid artery which is closed to external branch of superior laryngeal nerve, pierces thyroid fascia and divide into anterior supplying anterior surfaces, posterior branch supply lateral and medial surfaces.

The inferior thyroid artery reaches base of gland and divides into superior and inferior branches to supply inferior and posterior surfaces of gland. Relationship between inferior thyroid artery and RLN is highly variable and consider clinical importance. Most reliable place to identify RLN is in Beahr's triangle where RLN, inferior thyroid and common carotid arteries.

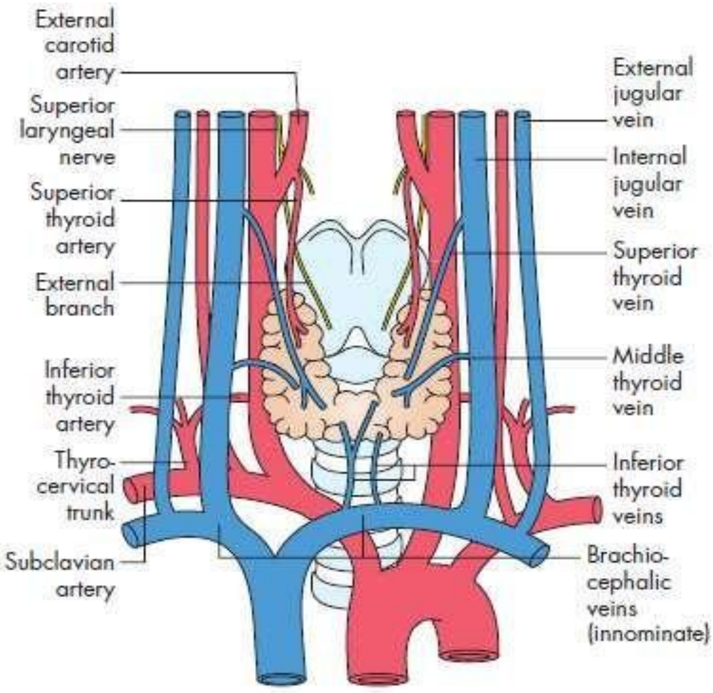


Fig.7-Blood supply

Veins:
The thyroid gland typically drains blood through the superior, middle, and inferior thyroid veins.
- The **superior thyroid veins** emerge from the upper part of the thyroid gland, running alongside the superior thyroid artery towards the carotid sheath, and drain into the internal jugular vein.
- The **middle thyroid veins** collect blood from the lower portions of the thyroid gland, emerging from its lateral surface, and also drain into the internal jugular vein.
- The **inferior thyroid veins** originate from the glandular venous plexus, which connects the superior and middle thyroid veins. These veins form the pretracheal plexus. From here, the left inferior thyroid vein descends to join the left brachiocephalic vein, while the right inferior thyroid vein descends obliquely across the brachiocephalic artery to join the right brachiocephalic vein at its junction with the superior vena cava.

Lymphatics:
Thyroid lymphatics vessels communicate within the gland and tracheal plexus, passing onwards to prelaryngeal node just above thyroid isthmus and then to pretracheal and paratracheal nodes (level vi). Some may drain into brachiocephalic node (level vii). Laterally it's drained to deep cervical nodes (level iv).
Majority is drained into middle (level iii), lower jugular (level iv) and posterior triangle (level v) lymph nodes

Innervation:
Thyroid gland receive its innervation from superior, middle, and inferior cervical sympathetic ganglia. Postganglionic fibres from inferior cervical ganglion form a plexus on inferior thyroid artery that accompanies artery to thyroid gland, communicates with recurrent laryngeal nerve and external branch of superior laryngeal nerves, superior cardiac nerve, plexus of common carotid artery.[5,6,7,8]

Embryology and Surgical Anatomy of Parathyroid Glands
The parathyroid glands develop from the third and fourth pharyngeal pouches of the endoderm, with additional contributions from the neural crest and ectoderm. At around six weeks, the pouch undergoes elongation. Initially hollow, the pouch later experiences cell proliferation, leading to solidification and subsequent migration.

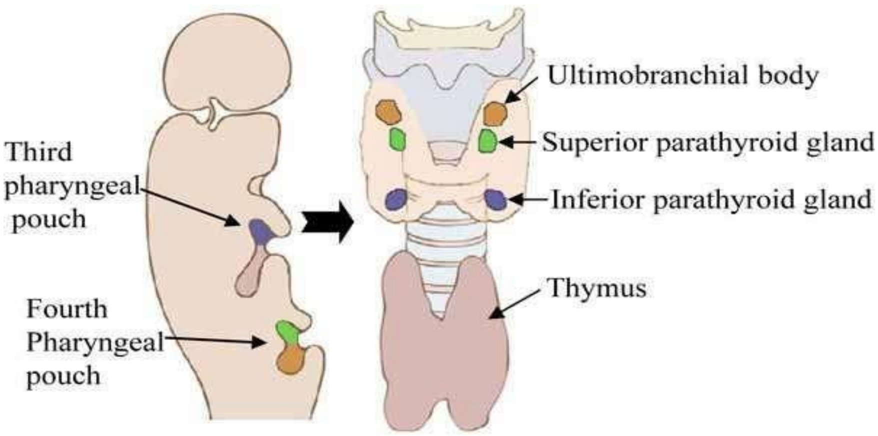


Fig.8 Embryology of Parathyroid gland

The inferior parathyroid glands originate from the third pharyngeal pouch, while the superior parathyroid glands arise from the fourth pharyngeal pouch. During fetal development, parathyroid hormone-producing cells respond to calcium levels, with fetal calcium level being higher than those of the mother.
Superior parathyroid glands: These glands derive from the fourth pharyngeal pouch. They are classically located near the posterolateral aspect of the superior pole of the thyroid, 1cm superior to

the junction of the recurrent laryngeal nerve (RLN), and the inferior thyroid artery. They classically lie deep to the plane of the recurrent laryngeal nerve.
Inferior parathyroid glands: These glands derive from the third pharyngeal pouch. These glands are classically located near the inferior poles of the thyroid glands, within 1-2 cm of the insertion of the inferior thyroid artery into the inferior pole of the thyroid. They classically lie superficial to the plane of the RLN. Their location is much more variable than the superior parathyroids, and can be intra-thyroidal or within the thymus or other mediastinal structures, and can even be found along the aortic arch.

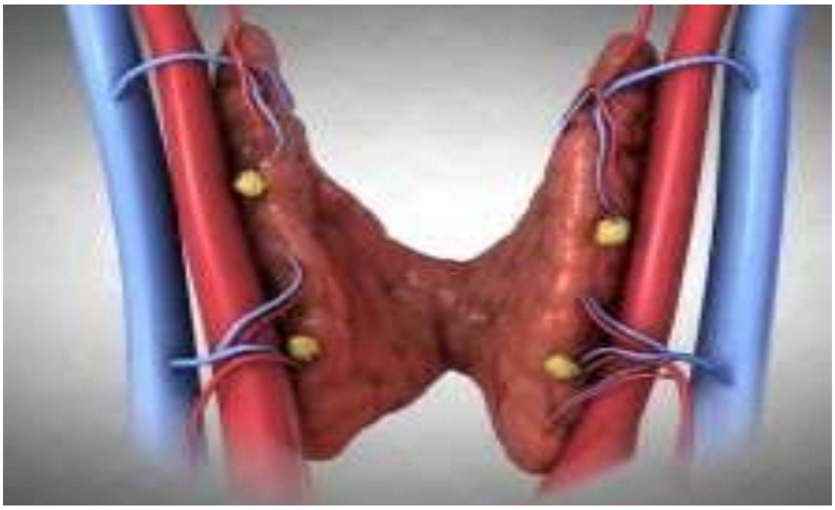


Fig.9-Blood supply of parathyroid Blood Supply and Lymphatics

The thyroid and parathyroid glands share a common blood supply. The inferior thyroid arteries provide blood to the parathyroid glands through their branches, typically supplying both the inferior and superior parathyroids. Additional collateral circulation is provided by the superior thyroid artery, thyroid ima artery, and branches from the laryngeal, tracheal, and esophageal arteries. The parathyroid veins drain into the thyroid venous plexus.

Lymphatic drainage from the parathyroid glands occurs via lymphatic vessels that lead to the deep cervical and paratracheal lymph nodes.

Nerves

The parathyroid glands receive their nerve supply from branches of the cervical ganglia associated with the thyroid gland. This innervation is primarily vasomotor, regulating blood flow to the parathyroid glands. [9]

ABOUT CALCIUM:

Calcium plays a crucial role in a variety of cellular functions, both inside and outside cells. Its functions can be broken down into two main categories:

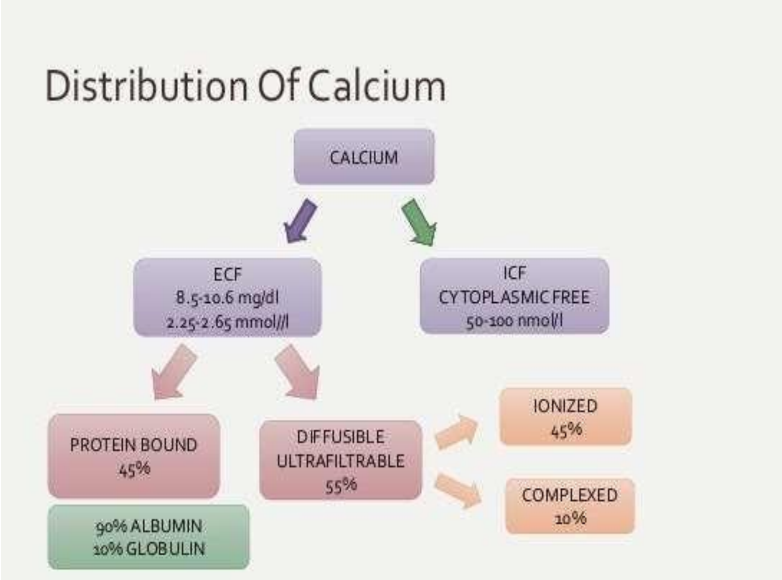


Fig.10-Calcium distribution

1. Intracellular Signalling: Calcium acts as a second messenger in many signalling pathways. It regulates processes like muscle contraction, neurotransmitter release, gene expression, and cell division. Calcium ions are involved in activating enzymes, altering protein functions, and influencing activity of ion channels, all of which help cells respond to stimuli and carry out their functions effectively.

2. Extracellular Functions: Calcium also plays a critical role outside cells, particularly in the maintenance of bone structure and in blood clotting. The majority of the body‘s calcium is stored in bones and teeth, providing structural integrity. In the blood, calcium is essential for coagulation, as it activates certain clotting factors that prevent excessive bleeding.

Because calcium is so important, the body tightly regulates its levels through systems involving the kidneys, bones, and intestines.
These three hormones—**1,25-Dihydroxycholecalciferol (the active form of vitamin D), Parathyroid hormone (PTH), and Calcitonin**—work together to regulate calcium homeostasis in the body.

1. **1,25-Dihydroxycholecalciferol (Active Vitamin D)**:
   - **Formation**: This steroid hormone is produced in the liver and kidneys. Initially, vitamin D is synthesized in the skin through exposure to sunlight and then converted to its active form through successive hydroxylations in the liver and kidneys. The liver converts vitamin D into **25-hydroxyvitamin D**, and the kidneys then convert it into **1,25-dihydroxyvitamin D** (also known as calcitriol), which is the hormonally active form.
   - **Primary Action**: The main role of calcitriol is to increase the absorption of calcium from the **intestines**. It promotes the expression of calcium-binding proteins in the intestinal lining, which enhances the active transport of calcium from the lumen of the intestine into the bloodstream.

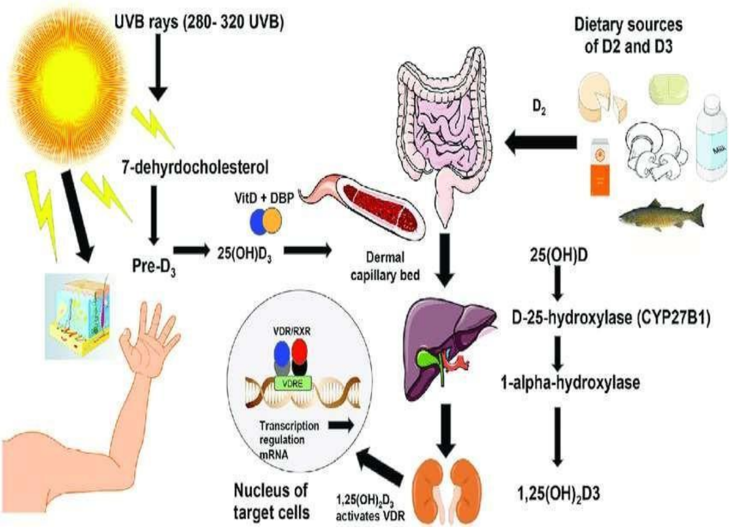


Fig.11-Vit D

Parathyroid Hormone (PTH):

- **Formation**: PTH is secreted by the **parathyroid glands**
- **Primary Action**: PTH is a key regulator of calcium and phosphate levels in the blood. It increases the concentration of calcium in the blood by:
  - **Mobilizing calcium from bone**: PTH stimulates **osteoclasts**, the cells responsible for breaking down bone tissue, which releases calcium and phosphate into the bloodstream.
  - **Increasing calcium reabsorption in the kidneys**: PTH reduces the excretion of calcium through urine.
  - **Increasing phosphate excretion**: It also reduces the reabsorption of phosphate from the kidneys, leading to an increase in urinary phosphate excretion. This is important because high phosphate levels can lead to calcium precipitation in tissues, which could impair calcium‘s physiological roles.

2. **Calcitonin**:

- **Formation**: Calcitoninis produced by the **C cells** (parafollicular cells) in the thyroid gland.
- **Primary Action**: Calcitonin is considered as calcium-lowering hormone. Its main effect is to **inhibit bone resorption** by osteoclasts, which decreases the release of calcium from bone into the bloodstream. Additionally, calcitonin helps increase calcium excretion by the kidneys.

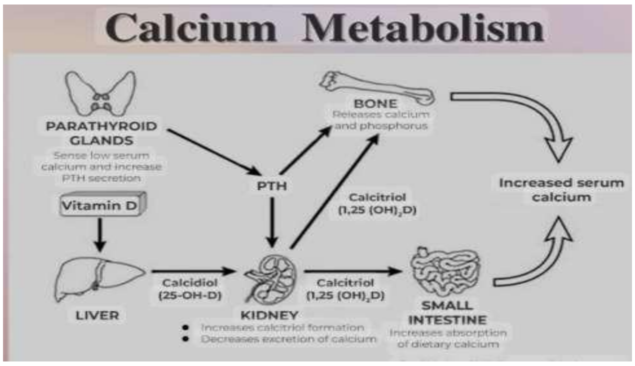


Fig.12-Calcium metabolism Total Calcium Content in the Body:

- The **body of a young adult human** contains approximately **1100 grams**(about **27.5 mol**) of calcium.
- **99% of this calcium is stored in the skeleton** (bones and teeth), which serves as a **reservoir** for calcium. The bones act as a storage site, releasing calcium into the bloodstream when needed, regulated by hormones such as **PTH** and **vitamin D**.
- The remaining **1% of calcium** is found in other tissues and fluids, including the **plasma** (blood)

and intracellular fluid.

Plasma Calcium Concentration:

- The **plasma calcium concentration** is tightly regulated and usually maintained at a normal level of about **10 mg/dL** (which is equivalent to **5 mEq/L** or **2.5 mmol/L**).**Plasma calcium exists in two forms**:

1. **Bound to plasma proteins (mostly albumin)**: Approximately **40- 45%** of the plasma calcium is bound to proteins, particularly albumin. This bound calcium is not readily available for biological processes, but it helps maintain the calcium pool.
2. **Free (ionized) calcium**: About **50-55%** of calcium in the plasma exists in an **ionized form (Ca^{2+})**, which is biologically active and can participate in various physiological functions.
3. **Complexed to other substances**: A small portion of calcium (around **5-10%**) is bound to anions like phosphate or bicarbonate, making it unavailable for cellular functions but still contributing to the overall calcium pool.

Role of Calcium in Plasma:

- The ionized calcium (Ca^{2+}) in the plasma is vital for:

o **Muscle function**: Calcium ions play a key role in muscle contraction, including the heart (cardiac muscle) and skeletal muscles.

o **Nerve transmission**: Calcium ions are essential in neurotransmitter release at synaptic junctions.

o **Blood clotting**: Several steps in the clotting cascade rely on calcium ions to form blood clots and stop bleeding.

o **Supportive structure**: Supporting material in skeletal system

Regulation of Plasma Calcium Levels:

To keep calcium levels in the plasma within a narrow range, the body utilizes several mechanisms:

1. **Hormonal Regulation**: **PTH**, **vitamin D**, and **calcitonin**
2. **Calcium Sensing**: The body has **calcium-sensing receptors** (CaSRs), primarily located in the parathyroid glands and kidneys, that detect changes in plasma calcium levels. When calcium levels drop, PTH is secreted to increase calcium levels. Conversely, when calcium levels rise, calcitonin is released to reduce calcium levels.
3. **Bone as a Calcium Reservoir**: The bones serve as a calcium reservoir. When blood calcium levels are low, bone resorption is stimulated to release calcium. When blood calcium levels are high, bone formation is stimulated to store calcium.

Parathyroid Hormone (PTH):

- **Structure**: **PTH** is a **peptide hormone** consisting of **84 amino acids**.
- **Regulation**: PTH secretion is regulated primarily by **serum calcium** levels, and it is not directly controlled by the pituitary gland. In fact, **serum calcium levels** exert through negative feedback on PTH secretion: when calcium levels are low, PTH secretion increases; when calcium levels are high, PTH secretion is suppressed.

Actions of Parathyroid Hormone:

PTH has several key effects on the body that help increase **serum calcium levels**:

1. **Mobilization of Calcium from Bone**:

o **Bone Resorption**: PTH stimulates **osteoclasts**, cells that break down bone tissue and releases calcium and phosphate into the bloodstream, raising blood calcium levels.

2. **Increased Calcium Reabsorption in the Kidneys**:

o PTH acts on the **renal tubules**, enhancing calcium reabsorption, calcium is retained in the blood .

3. **Enhanced Phosphate Excretion in the Kidneys**:
4. PTH also reduces the reabsorption of **phosphate** in the kidneys, leading to increased excretion of phosphate in the urine as high phosphate levels can lead to calcium precipitation and interfere with

normal calcium function.**Increased Calcium Absorption from the Gastrointestinal Tract**:
o PTH indirectly increases the absorption of calcium from the **gastrointestinal (GI) tract** by stimulating the activation of **vitamin D** (in its active form, **1,25-dihydroxyvitamin D**). This active form of vitamin D promotes calcium absorption in the intestines.

Overall, these actions of PTH work together to raise serum calcium level [10,11] **Absorption of Calcium:**
Calcium is absorbed in the intestine, where it is first bound to **calbindin**, a calcium-binding protein. Once bound, calcium is transferred into the endoplasmic reticulum of the intestinal epithelial cells. From there, the **PMCA1 (plasma membrane calcium ATPase 1)** pump transports the calcium into the bloodstream.

Active Transport:
The major and active transport of calcium primarily occurs in the **duodenum**.

Passive Transport:
Calcium absorption also occurs passively in the **jejunum** and **ileum**.

The absorption of calcium is regulated by **calcitriol**, the active form of Vitamin D, in the blood. In response to parathyroid stimulation, **cholecalciferol (Vitamin D3)** is converted into **1,25-dihydroxycholecalciferol (calcitriol)** in the kidneys, which in turn regulates calcium absorption in the gastrointestinal tract (17).
The total calcium levels can be affected by serum protein (albumin) levels. Ionized calcium, however, is not influenced by serum albumin and is considered a more accurate measure, especially in cases of hypocalcemia. Therefore, the estimation of ionized calcium is generally more reliable than total calcium in assessing calcium status. In individuals with normal serum albumin levels, the total calcium level will generally reflect the biological effects of calcium. However, in cases where serum albumin is abnormal, the total calcium level may not accurately represent the true calcium status, since calcium binds to albumin. In these situations, a corrected calcium value is calculated to adjust for albumin variations.

For calculation of corrected calcium:
The formula used is:

Corrected Calcium (mg/dL) = Measured Total Calcium (mg/dL) + 0.8 × (4.0 - Serum Albumin in g/dL)
This equation helps to adjust the total calcium level, accounting for the difference in albumin concentration, and provides a more accurate reflection of the biologically active calcium. [10,11]

HYPOCALCEMIA
Hypocalcemia Definition:
- **Serum Calcium Level:** Below 8.5 mg/dL (2.12 mmol/L).
- **Ionized Calcium Level:** Below 4.6 mg/dL (1.15 mmol/L).
- **Normal values:**8.5-10.5mg/dl (2.12-2.62mmol/L) [10,11]

Signs and Symptoms of Hypocalcemia:
1. **Neurological Symptoms:**
   - Seizures,dementia
   - Emotional disturbances such as anxiety or depression
   - **Chvostek's Sign:** Tapping on the angle of the jaw over the facial nerve causes twitching of the facial muscles it innervates.

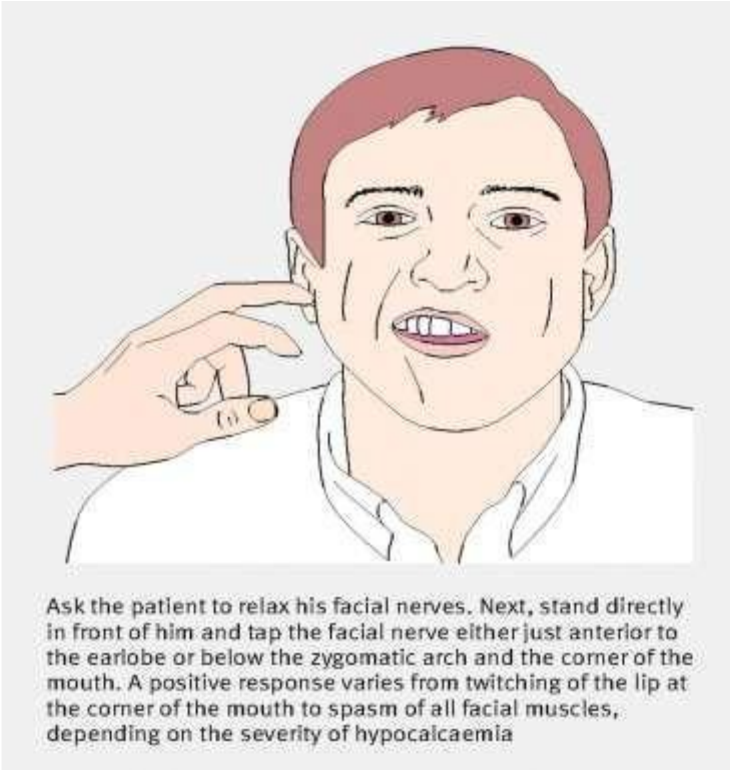


Fig.13-Chovstek sign

Trousseau's Sign:

- Induced carpopedal spasm by inflating a blood pressure cuff around the arm.
- Paresthesia in the extremities, perioral area
- Myalgias and muscle spasms
- Tetany or carpopedal spasm, including the "thumb-in-palm" deformity or "obstetrician‘s hand"

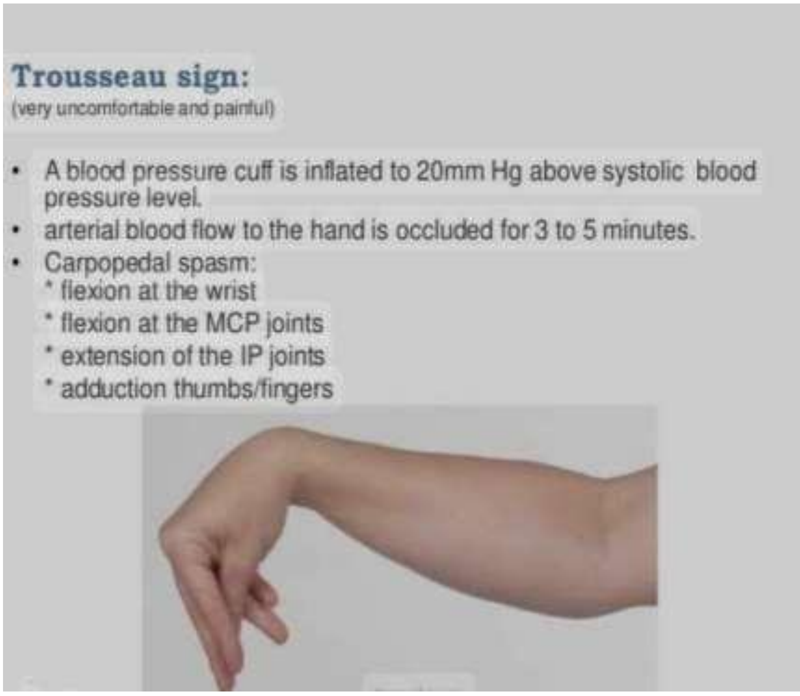


Fig.14-Trousseau sign

2. **Cardiovascular Symptoms:**

- **ECG Changes:** Prolonged QT interval
- Hypotension

- o Cardiac failure

3. **Autonomic Symptoms:**

- o Biliary colic
- o Bronchospasm
- o Diaphoresis (excessive sweating) [10]

Classification of Hypocalcemia

- **Based on Symptoms:**

1. **Asymptomatic**
2. **Moderate hypocalcemia**: Includes numbness, tetany, Chvostek's sign, Trousseau's sign**Severe hypocalcemia**: Seizures, ECG changes (QT prolongation), bronchospasm, laryngospasm, carpopedal spasm [12]

- **Based on Duration:**

1. **Temporary hypocalcemia**: Lasts less than 6 months
2. **Permanent hypocalcemia**: Lasts more than 6 months [13]

Management of Hypocalcemia:

- **For Asymptomatic Hypocalcemia:**

Start with **oral calcium replacement**, beginning with a low dose. Titrate according to 24-hour serum calcium assessment.

- **For Moderate Hypocalcemia:**

Patients can be treated in a general ward with an initial high dose of oral calcium, along with **calcitriol supplementation** (0.5 micrograms daily).

- **For Severe Hypocalcemia:**

Treatment should occur in the **Intensive Care Unit (ICU)**. Administer **intravenous calcium gluconate (10 mL diluted in 100 mL normal saline)** over **15 minutes** slowly. Monitor serum calcium levels frequently, along with continuous cardiac monitoring. Once normocalcemia is achieved, switch to **oral calcium supplementation** with Vitamin D [12,13,14]

THYROIDECTOMY

The aim of thyroidectomy is to remove the entire thyroid lobe (bilateral if total thyroidectomy), encompassing all disease and preserving the cervical strap muscles, external branches of superior laryngeal nerve, recurrent laryngeal nerve, parathyroid glands and their blood supply.

TECHNIQUE:

Anesthesia and positioning

The patient, under general anesthesia, is positioned supine with both arms tucked at the sides. The back is elevated, and the neck is extended by placing a soft roll behind the scapulae, with the head resting on a foam or gel ring. This positioning helps lift the thyroid gland to a more anterior and superior location in the neck. The operative field is then prepared, extending from the lower lip to the upper chest.

Incision and exposure of the Thyroid

A centrally placed transversed incision is made between sternal notch and cricoid cartilage, with effort to placed incision in normal skin line of the neck. The incision is extended through the platysma muscle and subplatysmal flaps are raised upto thyroid cartilage and superiorly and sternal notch inferiorly.

The strap muscles are seperated in the midline, sternohyoid is separated from sternothyroid. And sternothyroid is dissected from underlying thyroid capsule

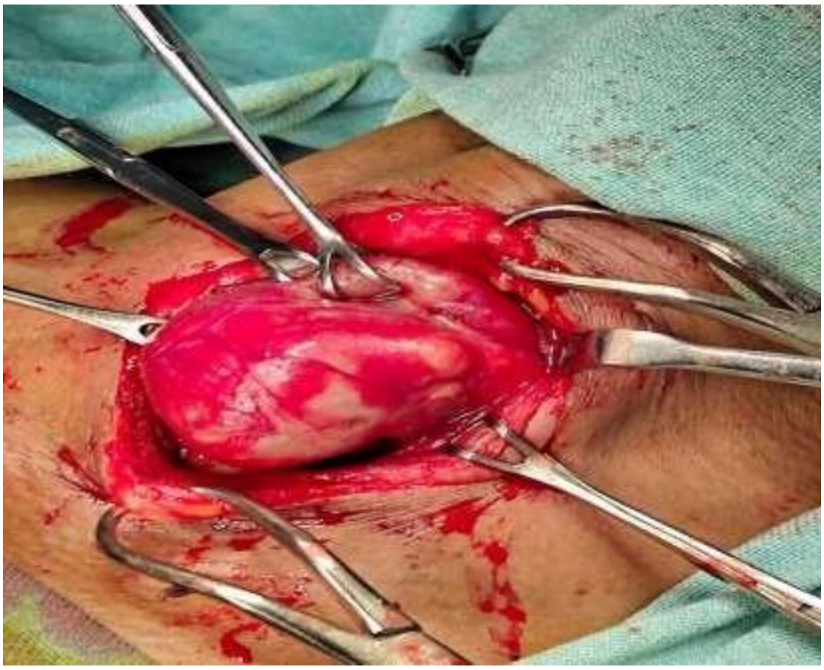


Fig.15-Exposure of Thyroid gland Dissection and release of the superior pole

Superior pole attachments are separated from surrounding muscles and exposed bluntly with peanut sponge. Exposures maneuvers are carried out superolaterally, posteriorly, with downward and lateral countertraction of thyroid glands. After exposing superior pole vessels, the lateral tissues are carefully mobilised to below the level of thyroid muscle, as RLN passes through Berry ligament and dives deep into laryngeal insertion point at level of cricoid cartilage. Superior pole is separated from cricothyroid muscle medially. Avascular plane or space of Reeves help on progressive dissection of superior pole vessels. These vessels are individually isolated, ligated and divided. Superior parathyroid gland is often identified behind mid- superior pole approximately at cricoid cartilage.

Mobilization of inferior pole and medial rotation of the Thyroid lobe

These mobilization includes identification of inferior parathyroid gland. Inferior parathyroid gland grasped with Allis forceps retracted anteromedially, inferior pole vessels entering anterolateral to tracheal surface are ligated and divided. Thyroid is progressively rotated and delivered in anteromedial direction.

The inferior parathyroid glands are identified and dissected away from thyroid gland.

Identification of the RLN and completion of Lobectomy

After superior and inferior attachments are freed, it‘s delivered in anteromedial rotation and retraction. Judicious retraction sis performed. Two commonly used rules of thumb for RLN identification it is located within 1cm anteromedial to superior parathyroid , at the level where nerve cross inferior thyroid artery and its course through Berry ligament is also situated just underneath and medial to tubercle of Zuckerkandl. Once parathyroids and RLN are identified and preserved, the remainder of thyroid gland are dissected away.

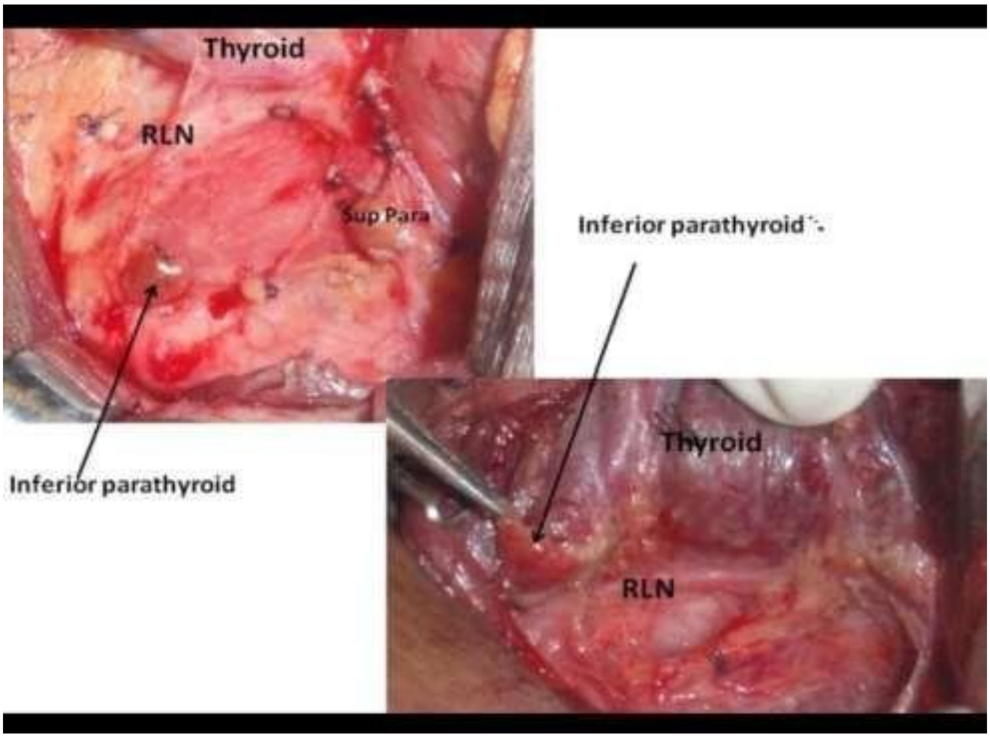


Fig.16-Intra op field

Closure

Meticulous hemostasis achieved. Sternothyroid and sternohyoid muscles are approximated with absorbable sutures with small left in lower midline to facilitate any blood to exit, platysma is reapproximated, skin closed [15,16,17]

Complications of Total Thyroidectomy

1. **Wound Hematoma**
   - An early, life-threatening complication that can result in airway obstruction.
   - May require immediate surgical intervention to relieve pressure and prevent further complications.
2. **Hypocalcemia**
   - Can be **temporary** or **permanent**.
   - Requires early diagnosis and prompt treatment to avoid severe symptoms.
3. **Seroma Collection**
   - Accumulation of fluid in the surgical area, often requiring drainage.
4. **Infection**
   - Possible infection at the surgical site, which can lead to complications and delayed healing.
5. **Hypertrophic Scar or Keloid**
   - Abnormal scarring that can affect cosmetic appearance and cause discomfort.
6. **Recurrent Laryngeal Nerve Palsy**
   - Injury to the recurrent laryngeal nerve can lead to vocal cord paralysis, causing hoarseness, or difficulty swallowing.
7. **Superior Laryngeal Nerve Palsy**
   - This damage can affect pitch and voice quality, particularly the ability to raise the pitch.
8. **Horner's Syndrome**
   - A rare complication that may result from injury to sympathetic nerves, leading to ptosis (drooping eyelid), miosis (constricted pupil), and anhidrosis (loss of sweating).
9. **Loss of Voice**
   - Due to damage to the vocal cords, this can result from recurrent laryngeal nerve injury, leading to hoarseness or even complete loss of voice.

10. Tracheomalacia

- Softening or collapse of the trachea, which may cause breathing difficulties.

11. Hypothyroidism

- A common outcome following total thyroidectomy due to the removal of the entire thyroid gland, leading to the need for lifelong thyroid hormone replacement therapy.

12. Airway Obstruction

- Can occur due to swelling, hematoma, or other postoperative complications, requiring urgent attention to maintain airway patency [15,16,18]

Factors Increasing the Incidence of Post-Thyroidectomy Complications:

1. **Extent of the Disease (Large Size)**

o Larger tumors or extensive disease increases the complexity of the surgery, leading to a higher risk of complications.

2. **Extent of the Surgery (Long Duration and Difficult Recovery from Anesthesia)**

o Prolonged surgeries and difficult recovery from anesthesia can increase the risk of complications such as infections, hematomas, and other postoperative issues.

3. **Extrathyroidal Extension of Disease**

o When the thyroid cancer or disease extends beyond the thyroid capsule, it can complicate the surgery, making it more challenging to remove the tissue entirely and increasing the risk of nerve or vascular damage.

4. **Surgeries Combined with Neck Dissection**

5. When thyroidectomy is performed alongside neck dissection, which involves removing lymph nodes, the risk of complications increases due to the additional dissection and the complexity of the surgery.

Reexploration for Postoperative Hematoma

o If a hematoma forms after surgery, it may require reexploration to evacuate the blood collection, which can increase the risk of additional complications, including infection, nerve damage, or further bleeding [39,41]

PREDICTORS OF HYPOCALCEMIA

Key Points on Calcium as a Predictor of Post-Thyroidectomy Hypocalcemia:

1. **Serial Calcium Estimations:**

o **Postoperative Monitoring**: Serial measurement of serum calcium levels has been widely studied as a predictor of hypocalcemia. This method can be especially helpful for clinicians when monitoring patients who may not have access to PTH testing. Calcium levels provide an easily accessible and affordable means of assessing calcium metabolism after surgery.

2. **Study by Ancuta Leahu et al.:**

o **Positive Calcium Trend**:The patients with a **positive calcium trend**— i.e., an increase in calcium levels on serial measurements of serum calcium shows normocalcemic, successfully excluding hypocalcemia on 99.2% patients. This finding highlights the usefulness of a **rise in calcium levels** as a reliable sign of recovery and a low risk of hypocalcemia, allowing for earlier discharge of patients without the need for prolonged monitoring or calcium supplementation.

3. **Negative Calcium Trend**: Conversely, a **negative calcium trend**, or a **decline in calcium levels** after surgery, was linked to a **51.6%** patients with chance of developing hypocalcemia. This suggests that patients with a falling trend in calcium levels should be carefully monitored for longer periods after surgery, and they may need further calcium supplementation to prevent or treat hypocalcemia.

Clinical Implications:

o **Discharge Decisions**: The positive calcium trend pattern can help guide **discharge decisions**. Patients who show a stable or increasing trend in calcium levels can be discharged earlier without significant concern for developing hypocalcemia.

o **Extended Monitoring**: On the other hand, patients with a falling calcium trend require **extended monitoring** or **calcium supplementation**, especially if it show signs or symptoms of hypocalcemia.

4. **Calcium Estimation in Resource-Limited Settings:**
o The **cost factor** of PTH estimation may make calcium monitoring a more practical option in **smaller healthcare setups** or low-resource environments. Since serum calcium levels are more widely available and less costly than PTH testing, routine calcium monitoring provides a feasible alternative for predicting hypocalcemia. [19,20,21,22,23,24,37]

Key Points on PTH as a Predictor of Post-Thyroidectomy Hypocalcemia:
1. **Intraoperative and Postoperative PTH Estimation:**
o **Intraoperative PTH Estimation**: Measuring PTH levels during surgery can help predict postoperative complications. A significant drop in PTH during surgery often indicates injury to or removal of the parathyroid glands, increasing the risk for hypocalcemia.
2. **Postoperative PTH Estimation**: Measuring PTH at 1 hour and 24 hours after surgery has been shown to be a reliable method for predicting post- thyroidectomy hypocalcemia. A fall in PTH levels at these intervals, especially a continuing decline, is a strong predictor of hypocalcemia (Lam and Ker et al.).

PTH Level Thresholds:
o **8 pg/mL as a Threshold**: A PTH level below 8 picograms per milliliter (pg/mL) is associated with a higher likelihood of developing hypocalcemia after thyroidectomy. This cutoff is a useful marker for anticipating calcium imbalances.
o **Above 9 pg/mL**: If the PTH level is above 9 pg/mL, the likelihood of hypocalcemia decreases significantly, indicating a better recovery of parathyroid function and less risk for hypocalcemia
o **Falling PTH Levels**: A continuing decline in PTH levels, particularly at the 1-hour and 24-hour postoperative time points, can indicate persistent or worsening parathyroid dysfunction and a heightened risk for hypocalcemia.
o **Cost and Availability**: While PTH estimation is a well-documented and effective predictor of hypocalcemia, its widespread use is limited by the availability and cost of the test, especially in smaller or resource-limited hospitals. This can restrict the routine use of PTH monitoring in some clinical settings. [25,26,43]
3. Similar study shows that PTH-1hour is a strong predictor for identifying patients at risk of hypocalcemia 24 hours after surgery. If PTH-1 levels fall below 1.5 pmol/L, preventive treatment with calcitriol should be initiated to prevent symptomatic hypocalcemia from developing. [27,28]

PREVENTION OF POST THYROIDECTOMY HYPOCALCEMIA

A multi-faceted process that involves careful surgical technique, good team coordination, and diligent postoperative management. Here's an outline of key strategies for prevention:

1. Surgeon’s Knowledge of Anatomy and Embryology

- **Thyroid and Parathyroid Anatomy**: A deep understanding of the **anatomy and embryology** of the thyroid and parathyroid glands is crucial for minimizing the risk of damage to the parathyroids during surgery.Surgeons need to be well-versed in the **variation of parathyroid gland locations** and structures to avoid accidental injury.

2. Surgical Team Coordination

- **Surgeon and Anaesthetist Rapport**: Effective communication between the **surgeon and anaesthetist** is vital to ensure smooth anesthesia management during the procedure. Such as **laryngeal edema**, which could affect parathyroid function indirectly by impairing airway management.

3. Endotracheal Tube Size

- **Proper Tube Size**: The **endotracheal tube** should have a **smaller cuff size** to prevent **laryngeal**

edema. This is crucial because laryngeal edema can increase the risk of complications like airway obstruction, which may complicate the surgical process and recovery.

4. Surgical Field and Exposure

- **Good Exposure and Lighting**: Ensuring **adequate exposure** and using a **good light source** will help in **visualizing** the thyroid and parathyroid glands.

5. Hemostasis

- **Perfect Hemostasis**: Proper **hemostasis** (control of bleeding) is crucial for **identifying the parathyroids** in the operating field.

6. Meticulous Dissection

7. Careful Dissection: Surgeons should perform **meticulous dissection** throughout the procedure to avoid damaging the parathyroids, especially when handling surrounding tissues or performing gland removal.

Identification of Parathyroid Glands

- **Recognizing Parathyroids**: The surgeon should be familiar with the **size, color**, and **location** of the parathyroid glands.

8. Protection of Blood Supply

- **Blood Supply to Parathyroids**: Protecting the **blood supply** to the parathyroids is critical. To ensure adequate perfusion, the surgeon should **ligate the inferior thyroid artery** at its terminal branch, which is often the primary source of blood to the parathyroid glands.

9. Parathyroid Autotransplantation

- **Auto-Transplantation**: If a parathyroid gland is injured or its blood supply is compromised, **immediate parathyroid autotransplantation** into the **same-side sternocleidomastoid muscle** should be performed. This helps preserve the parathyroid tissue and its function, reducing the risk of permanent hypocalcemia.

11. Postoperative Care and Monitoring

- **Close Postoperative Follow-Up**: Monitoring for **hypocalcemia** should continue closely in the postoperative period, especially in patients who may have a more chances of developing low calcium levels. Early **detection** and **management** of hypocalcemia can significantly reduce complications and improve recovery.

12. Calcium and PTH Monitoring: As mentioned earlier, serial calcium monitoring in the postoperative period is vital for identifying any developing hypocalcemia early, allowing for timely interventions such as **calcium supplementation**.

Patient Education and Management

- **Patient Education**: Patients should be educated about the signs and symptoms of hypocalcemia (e.g., numbness, tingling, muscle cramps, seizures) and instructed to seek medical help promptly if they experience these symptoms.
- **Early Supplementation**: Patients identified at high risk for hypocalcemia may require **oral calcium supplementation** immediately post-surgery to prevent or treat hypocalcemia. [4,13,14,15,16,30,42]

Parathyroid Auto-Transplantation

Ideally identification and preservation of parathyroid gland during surgery is critically important. If accidental removal of the parathyroid glands during thyroid surgery can result in **temporary or permanent hypocalcemia**. To prevent this life-threatening complication, some studies suggest that

auto-transplantation of the parathyroid glands into the **sternocleidomastoid muscle**. This procedure is performed whenever a surgeon identifies a **devitalized** or **devascularized parathyroid gland** during surgery.

The technique of **parathyroid auto-transplantation** was first described by **F.H. Lahey** in 1926. Parathyroid transplantation can be considered in three distinct modes of application:

(I) Fresh parathyroid tissue auto transplantation during thyroidectomy in order to reduce the risk of permanent hypoparathyroidism;
(II) Cryopreserved parathyroid tissue auto transplantation in patients with permanent hypocalcemia;
(III) Parathyroid allotransplantation in patients with permanent hypoparathyroidism when cryopreserved parathyroid tissue is not available for grafting [4,14,31,32,33,34,35,36]

MATERIALS AND METHODS

STUDY DESIGN

Prospective observational study

STUDY SETTING

Dept. of General Surgery, Govt.TD medical college, Alappuzha

STUDY PERIOD

One year from the start of study after institutional ethical board clearance

STUDY POPULATION

Patient who underwent total thyroidectomy in TDMCH, Vandanam, General Surgery dept.

INCLUSION CRITERIA

Any patient who fulfills all of the following criteria are included in the following study

1. Patient with clinically and pathologically diagnosed thyroid swelling who underwent total Thyroidectomy.
2. 18 years and above

EXCLUSION CRITERIA

1. Patient already on calcium supplementation.
2. Known Parathyroid disorders.
3. Previous irradiation to neck.
4. Thyroidectomy with neck dissection.
5. Chronic kidney disease

SAMPLE SIZE ESTIMATION

Sample size was calculated using the formula $N = (z)^2 p\,(1-p)/\,d^2$

Where, p = prevalence of hypocalcemia from previous study d = relative precision (20% of p)

$Z\alpha$=Z value correspond α significance N = minimum required sample size

According to study conducted sriVignesh et al [1] Substituting,

$Z\alpha=1.96$, $d= 20/100\times28$, $p=28$ N = 126

In our study setting, around 70-80 cases are available in a year, $n_0 = 80$

$n = N/\,(1 + N/n_0)$

= 49

SAMPLING METHOD

Consecutive sampling

Hypocalcemia in this study is defined as serum level of calcium less than 8.5mg/dl with clinical symptoms and signs.

DATA COLLECTION TOOLS

A structured questionnaire will be used to collect information from participants who have come for Thyroidectomy. It includes socio demographic profile, brief clinical findings, post-op serum calcium, symptoms, post op day, surgery and discharge, complications will be recorded.

DATA COLLECTION PROCEDURE

The investigator will explain aims of study, investigation required, timed required for participation. Those who give informed consent will be considered participants of study. They will be interview as part of study. Post thyroidectomy calcium level will be recorded and symptoms or without symptoms will be noted. Socio-personal details will be ascertained and recorded in study. Once surgery is done post operative events will be noted.

DATA ANALYSIS

The obtained data will be entered into the excel worksheet and analysis will be done using SPSS software version 27. Independent variables including patient factors, clinicopathological factors. Baseline differences of patients were evaluated using chi-squared test for categorical data and independent sample t test for continuous data. Univariate logistic regression was applied to identify key predictors of incidence of post thyroidectomy hypocalcemia.

ETHICAL CONSIDERATIONS

The above mentioned study will be conducted in this institution after obtaining due ethics clearance from the Institutional Ethics Committee of Government TD Medical College, Alappuzha. Informed consent will be obtained from the participants. Confidentiality of the patient will be maintained during every stage of the study.

EXPECTED OUTCOME OF STUDY

By analyzing the occurence of hypocalcemia after total thyroidectomy, we will be able to identify subset of patients developing hypocalcemia based on different pathology. Thereby we can effectively counsel the pre operative patients and analytical study can be performed to assess the incidence. Factors associated with these symptoms will also be found out.

RESULTS

Age (n=49)

Variable	Mean ± SD	Median (Q1, Q3)	Minimum	Maximum
Age (Yr)	49.18 ± 10.60	49 (43.50,58)	19	69

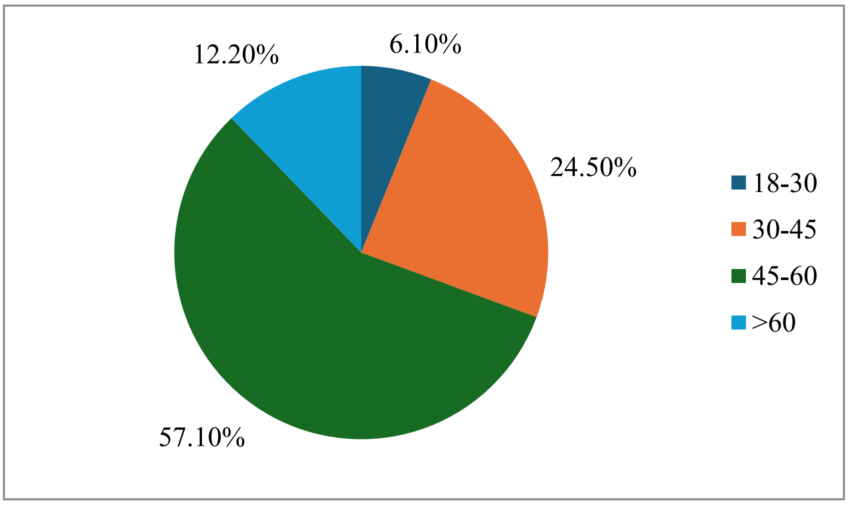
Age Group

We categorize study population according to the distribution of age into four groups

Group 1:18-30 years
Group 2:30-45 years
Group 3:45-60 years
Group 4:More than 60 years

Table 1:Age group

Age Group (yr)	Frequency	Percentage
18-30	3	6.1%
30-45	12	24.5%
45-60	28	57.1%
>60	6	12.2%
Total	49	100%



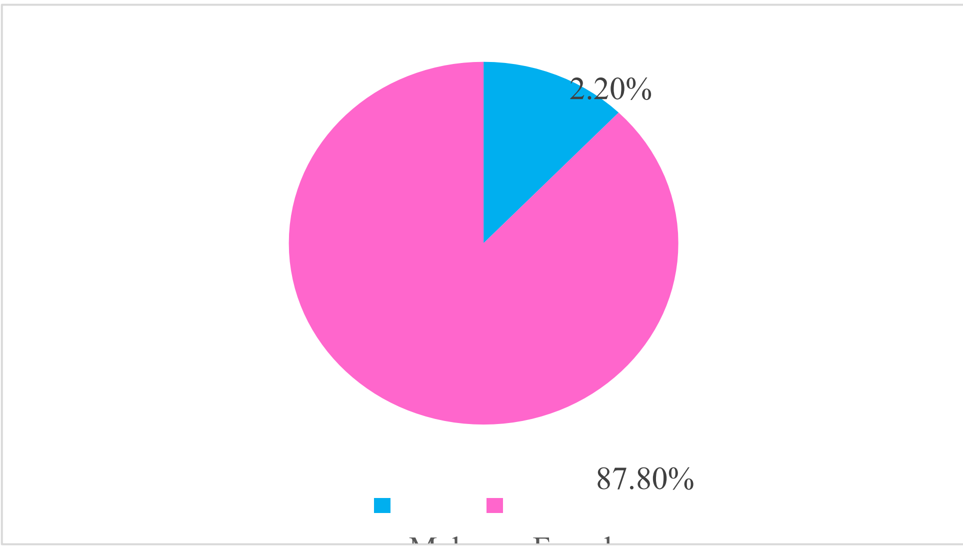
Graph 17:Age group

3 Patients fall in group 1, 12 patients fall in group 2, 28 patients fall in group 3, 6 patients fall in the group 4.

Gender

Table 2:Gender

Gender	Frequency	Percentage
Male	6	12.2%
Female	43	87.8%
Total	49	100%



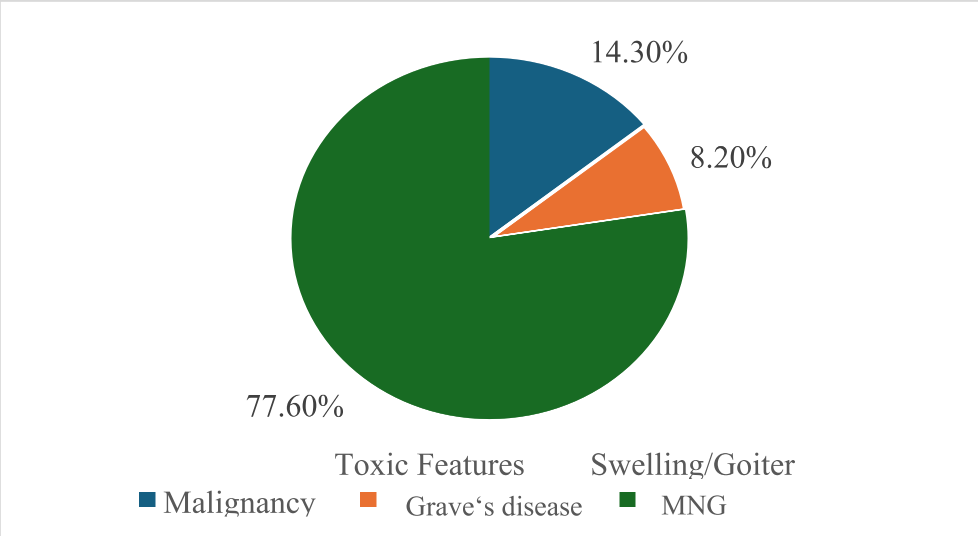
Graph 18:Gender

In our study we followed 49 patients and 43 were female and 6 were male

Preoperative Indications for Total Thyroidectomy

Table 3: Preoperative indication for total thyroidectomy

Preoperative Indications for Total Thyroidectomy	Frequency	Percentage
Malignancy	7	14.3%
Grave's disease	4	8.2%
MNG	38	77.6%
Total	49	100%



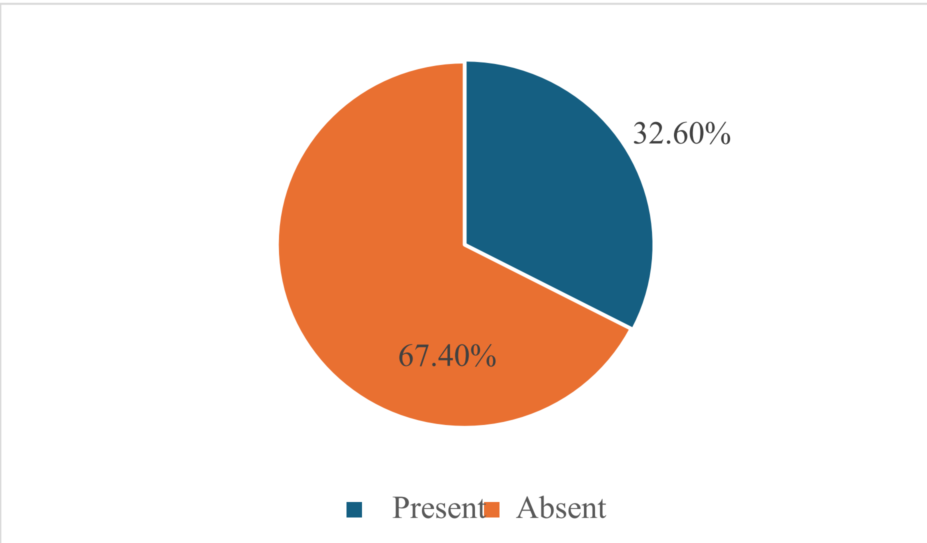
Graph 19:Preoperative indications for total thyroidectomy

As per pre op indications of the study MNG consists of 38 patients, 7 were malignancy and 4 are Graves' disease

Post Operative Hypocalcemia

Table 4;Post operative hypocalcemia

Post Operative Hypocalcemia	Frequency	Percentage
Present	16	32.6%
Absent	33	67.4%
Total	49	100%



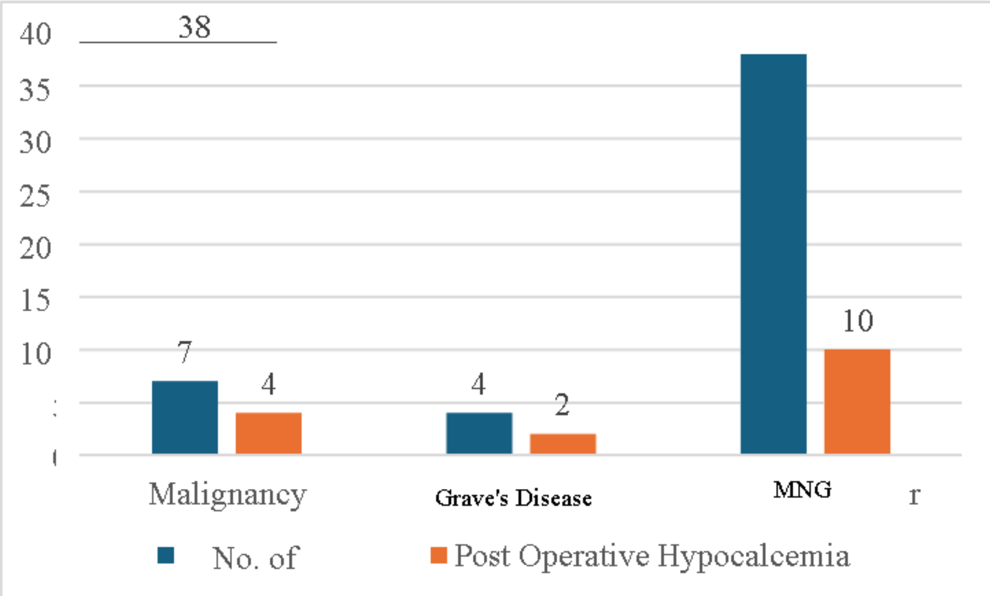
Graph 20:Post operative hypocalcemia

In my study 16 patients develop post op hypocalcemia out of 49 patients

Preoperative Indications for Total Thyroidectomy

Table 5:Preoperative indications for total thyroidectomy – Post OP hypocalcemia

Preoperative Indications for Total Thyroidectomy	No. of Patients (n)	Post Operative Hypocalcemia (n)	Percentage
Malignancy	7	4	57%
Grave‘s disease	4	2	50%
MNG	38	10	26%
Total	49	16	33%



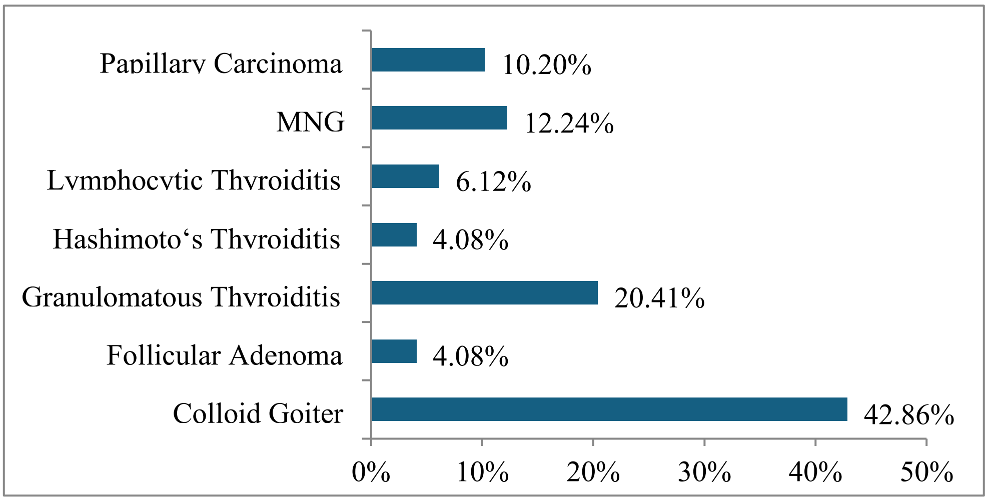
Graph 21:Preoperative indications for total thyroidectomy thyroidectomy – Post OP hypocalcemia

Out of 7 pre op malignancy indication 4 develops post op hypocalcemia, 2 out of 4 Graves‘ disease and 10 out of 38 MNG patients develop hypocalcemia

Post OP HPE

Table 6: Post op HPE

Post OP HPE	Frequency	Percentage
Colloid Goiter	21	42.86%
Follicular Adenoma	2	4.08%
Granulomatous Thyroiditis	10	20.41%
Hashimoto‘s Thyroiditis	2	4.08%
Lymphocytic Thyroiditis	3	6.12%
MNG	6	12.24%
Papillary Carcinoma	5	10.20%
Total	49	100%



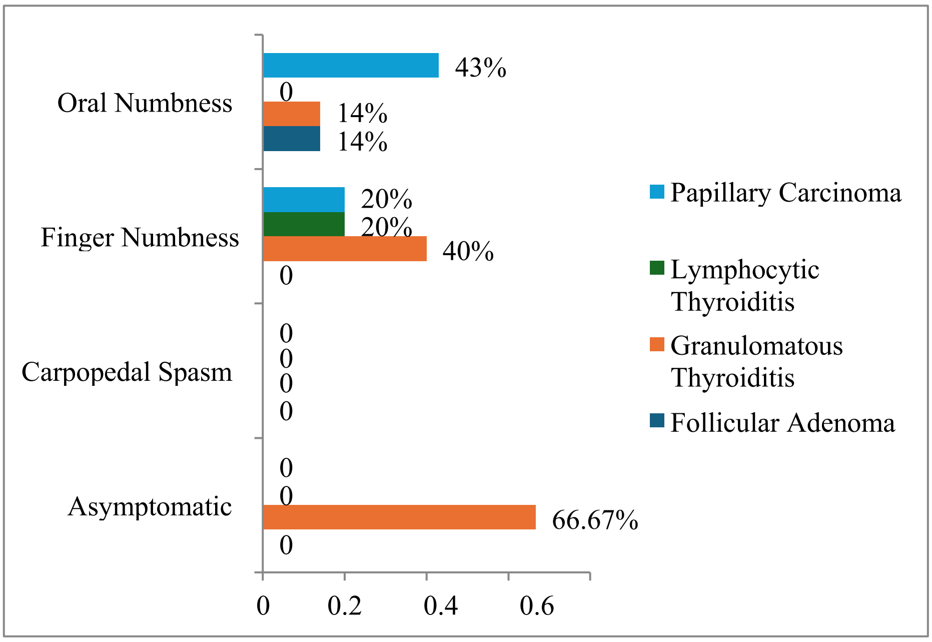
Graph 22:Post op HPE

Post op follow up shows the following HPE reports.
21 patients colloid goiter, 2 patients follicular adenoma, 10 patients granulomatous thyroiditis, 2 Hashimitos thyroiditis, 6 multinodular goitre, 3 lymphoctic Thyroiditis and 5 papillary carcinoma.

Post Operative Hypocalcemia – Post OP HPE

Table 7: Post Operative Hypocalcemia – Post OP HPE

Post OP HPE	**Asymptomatic n (%)**	**Carpopedal Spasm n (%)**	**Finger Numbness n (%)**	**Oral Numbness n (%)**
Colloid Goitre	1 (33.33%)	1 (100%)	1 (20%)	2 (29%)
Follicular Adenoma	0	0	0	1 (14%)
Granulomatous Thyroiditis	2 (66.67%)	0	2 (40%)	1 (14%)
Lymphocytic Thyroiditis	0	0	1 (20%)	0
Papillary Carcinoma	0	0	1 (20%)	3 (43%)
Total	3 (100%)	1 (100%)	5 (100%)	7 (100%)



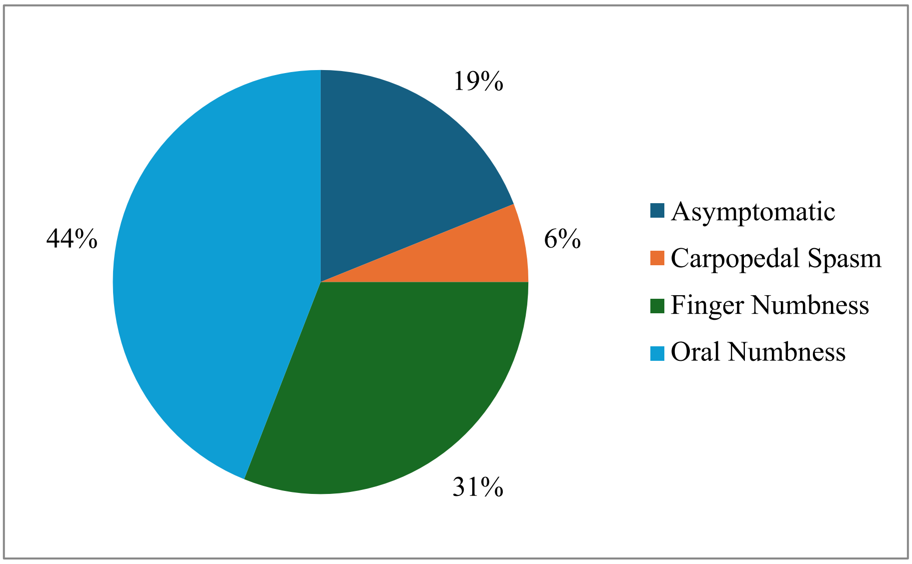
Graph 23: Post operative hypocalcemia-post op HPE

In relation to post op HPE and symptoms manifest we categorize
Colloid goitre: Asymptomatic 1, carpopedal spasm 1, finger numbness 1,oral numbness 2
Follicular adenoma:1 oral numbness Granulomatous thyroiditis: 2 asymptomatic, 2 finger numbness,1 oral numbness Lymphocytic thyroiditis:1 finger numbness
Papillary carcinoma: 1 finger numbness, 3 oral numbness

Symptoms

Table 8: Symptoms

Symptoms	Frequency	Percentage
Asymptomatic	3	19%
Carpopedal Spasm	1	6%
Finger Numbness	5	31%
Oral Numbness	7	44%
Total	16	100%



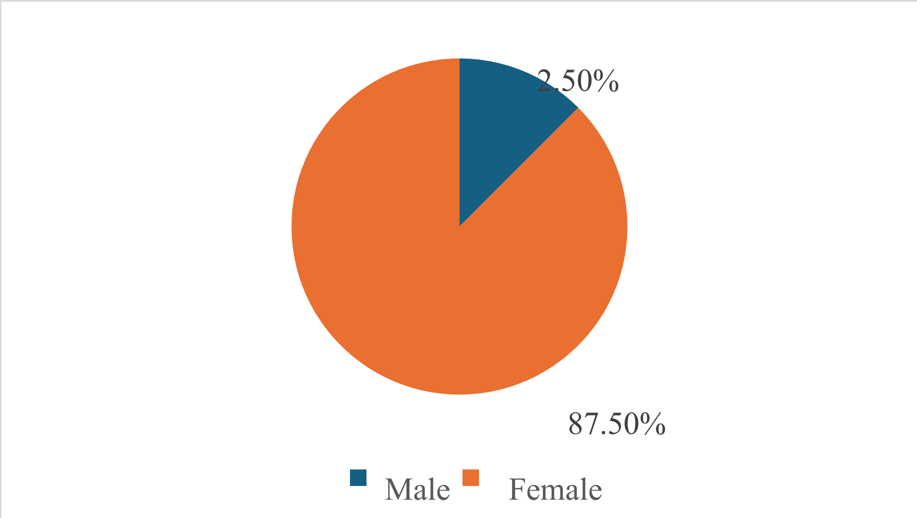
Graph 24:Symptoms

Out of different symptoms manifestation oral numbness constitute 44%, finger numbness 31%, carpopedal spasm 6%, asymptomatic 19%.

Post Operative Hypocalcemia – Gender

Table 9: Post Operative Hypocalcemia – Gender

Gender	Frequency	Percentage
Male	2	12.5%
Female	14	87.5%
Total	16	100%



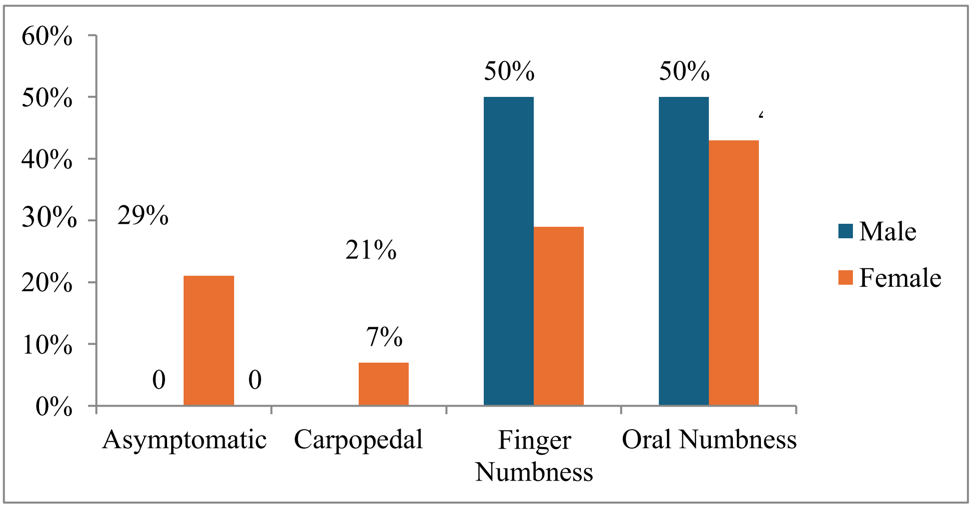
Graph 25 : Post operative hypocalcemia-Gender

Out of 16 patients showing hypocalcemia 2 are male and remaining 14 are female

Symptoms – Gender

Table 10: Symptoms – Gender

Symptoms	Male n (%)	Female n (%)
Asymptomatic	0	3 (21%)
Carpopedal Spasm	0	1 (7%)
Finger Numbness	1 (50%)	4 (29%)
Oral Numbness	1 (50%)	43 (43%)
Total	2 (100%)	14 (100%)



Graph 26:Symptoms with gender based

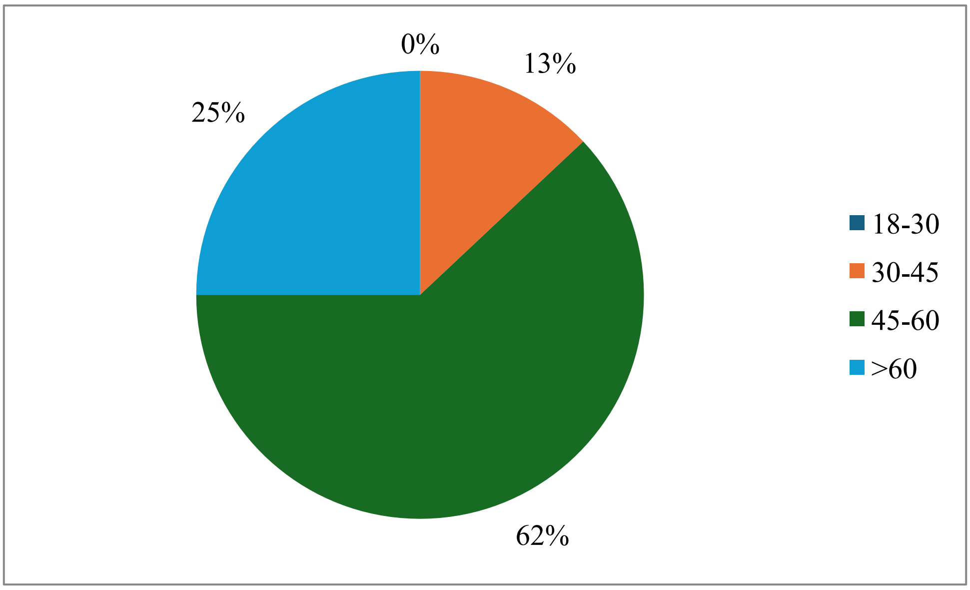
Symptoms with gender based:

Female-3 asymptomatic, 1 carpopedal spasm,4 finger numbness, 6 oral numbness Male-1 oral numbness, 1 finger numbness

Post Operative Hypocalcemia - Age Group

Table 11: Post Operative Hypocalcemia - Age Group

Age Group (yr)	Frequency	Percentage
18-30	0	0
30-45	2	13%
45-60	10	62%
>60	4	25%
Total	16	100%



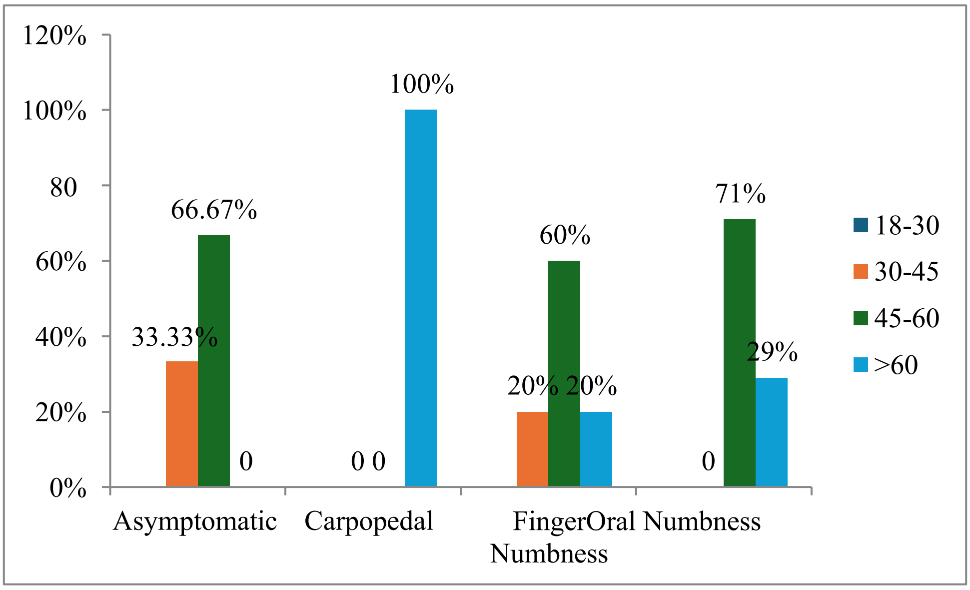
Graph 27:Post operative hypocalcemia-age group

According to age group and frequency of hypocalcemia Group 1: 0%
Group 2:13%
Group 3:62%
Group 4:25%

Symptoms - Age Group

Table 12: Symptoms - Age Group

Symptoms	Asymptomatic n (%)	Carpopedal Spasm n (%)	Finger Numbness n (%)	Oral Numbness n (%)
18-30	0	0	0	0
30-45	1 (33.33%)	0	1 (20%)	0
45-60	2 (66.67%)	0	3 (60%)	5 (71%)
>60	0	1(100%)	1 (20%)	2 (29%)
Total	3 (100%)	1(100%)	5 (100)	7 (100%)



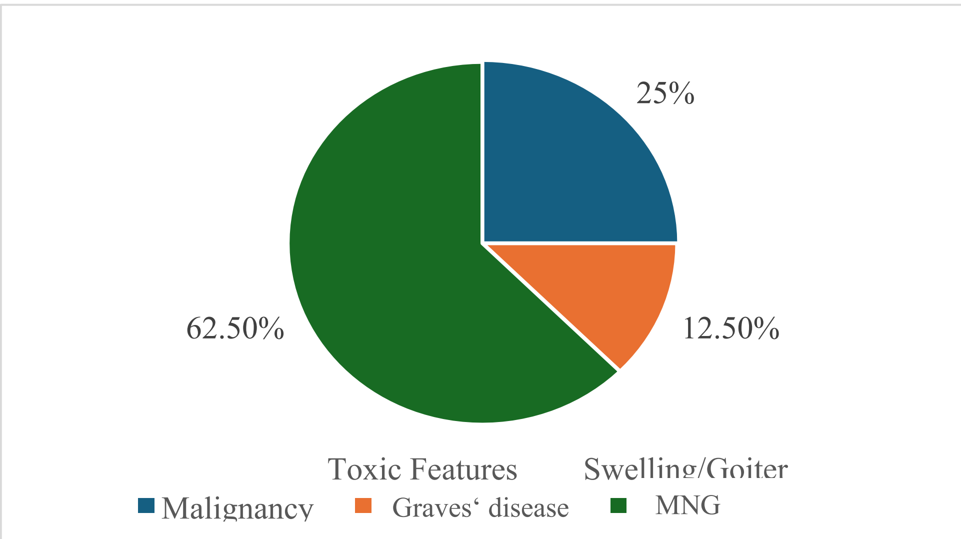
Graph 28:Symptoms-age group

Symptoms and age group Group 1: 0%
Group 2:1 asymptomatic, 1 finger numbness
Group 3: 2 asymptomatic, 3 finger numbness, 5 oral numbness Group 4:1 carpopedal spasm, 1 finger numbness, 2 oral numbness

Preoperative Indications - Post Operative Hypocalcemia

Table 13: Preoperative Indications - Post Operative Hypocalcemia

Preoperative Indications for Total Thyroidectomy	Frequency	Percentage
Malignancy	4	25%
Grave‘s disease	2	12.5%
MNG	10	62.5%
Total	16	100%



Graph 29:Pre operative hypocalcemia-Post operative age group

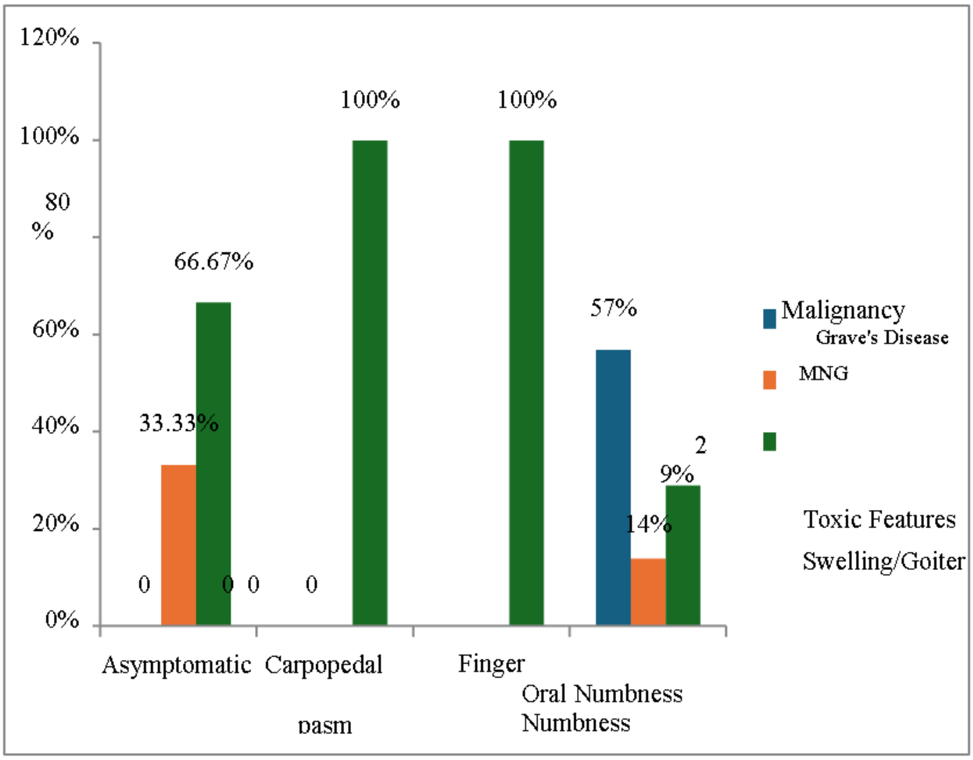
Out of all premalignant thyroidectomy indication 4 malignant patients develop hypocalcemia,2 Grave‘s disease, and 10 MNG.

Preoperative Indications - Post Operative Hypocalcemia

Table 14: Preoperative Indications - Post Operative Hypocalcemia

Preoperative Indications for Total Thyroidectomy	Asymptomatic n (%)	Carpopedal Spasm n (%)	Finger Numbness n (%)	Oral Numbness n (%)
Malignancy	0	0		4 (57%)
Graves‘ disease	1 (33.33%)	0	0	1 (14%)
MNG	2 (66.67%)	1 (100%)	5 (100%)	2 (29%)
Total	3 (100%)	1 (100%)	5 (100%)	7 (100)

Pre op indications with post op hypocalcemia

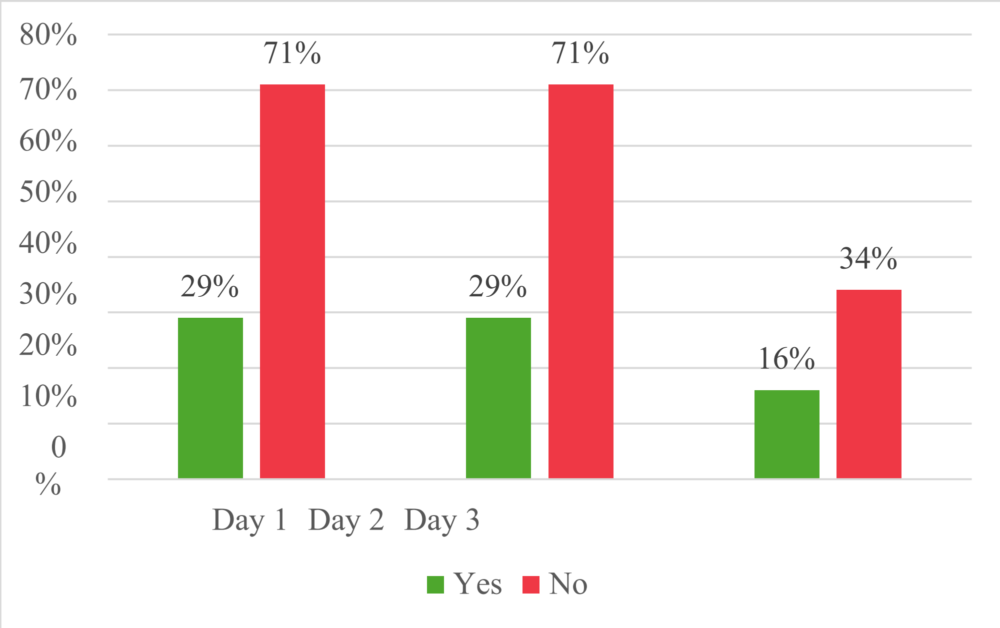


Graph 30:Pre operative indication-Post operative hypocalcemia

Proportion of Patients who Developed Hypocalcemia on Day 1, 2 & 3

Table 15: Proportion of Patients who Developed Hypocalcemia on Day 1, 2 & 3

Patients Who Developed Hypocalcemia	Day 1 n (%)	Day 2 n (%)	Day 3 n (%)
Yes	14 (29%)	14 (29%)	8 (16%)
No	35 (71%)	35 (71%)	41 (34%)
Total	49 (100%)	49 (100%)	49 (100%)



Graph 31:Proportion of hypocalcemia on post op day 1, 2,3

Post op hypocalcemia of total 49 patients Day 1:14 patients
Day 2:14 patients
Day 3:8 patients

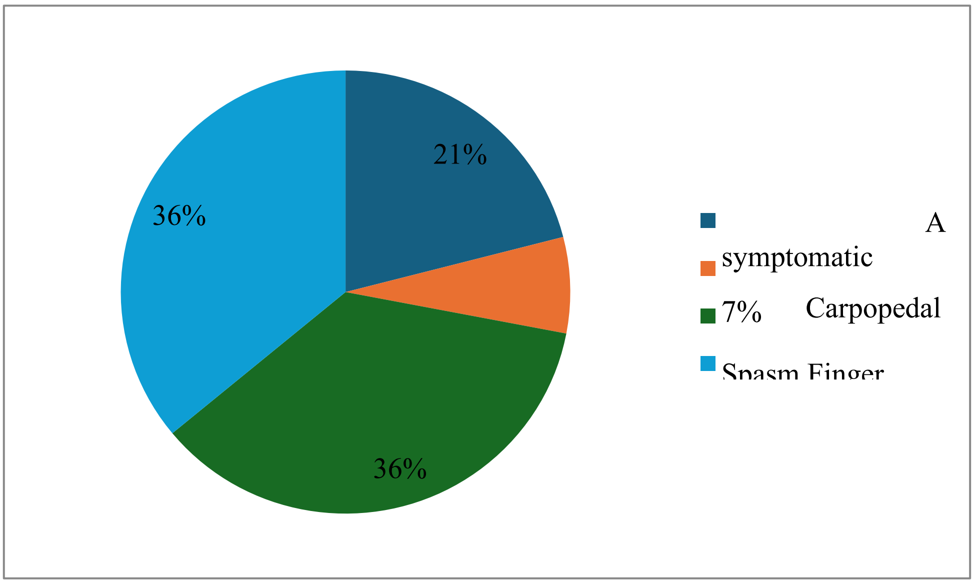
PROPORTION OF PATIENTS WHO DEVELOPED HYPOCALCEMIA ON DAY 1

Variable	**Mean + SD**	**Median (Q1, Q3)**	**Minimum**	**Maximum**
SERUM CA	8.11 + 0.26	8.20 (8.00,8.30)	7.3	8.4

Table 16: Manifested symptoms and frequency

Symptoms	**Frequency**	**Percentage**
Asymptomatic	3	21%
Carpopedal Spasm	1	7%
Finger Numbness	5	36%
Oral Numbness	5	36%
Total	14	100%

On post op Day 1: 3 asymptomatic,1 carpopedal spasm, 5 each for finger and oral numbness

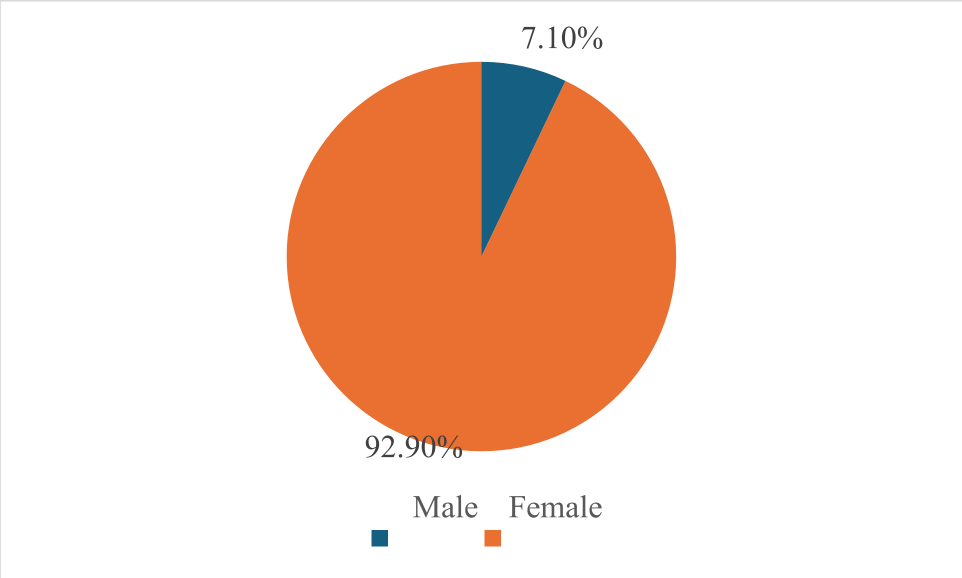


Graph 32:Manifested symptoms and frequency

Table 17:Gender and frequency

Gender	Frequency	Percentage
Male	1	7.1%
Female	13	92.9%
Total	14	100%

On post op day 1:1 patient is male and 13 are female



Graph 33:Gender and frequency

Table 18:Pre op indications and frequency of hypocalcemia

Preoperative Indications for Total Thyroidectomy	Frequency	Percentage
Malignancy	2	14.3%
Grave's disease	2	14.3%
MNG	10	71.4%
Total	14	100%

Pre op indication and frequency of hypocalcemia Malignancy 2, Grave's disease 2, MNG 10

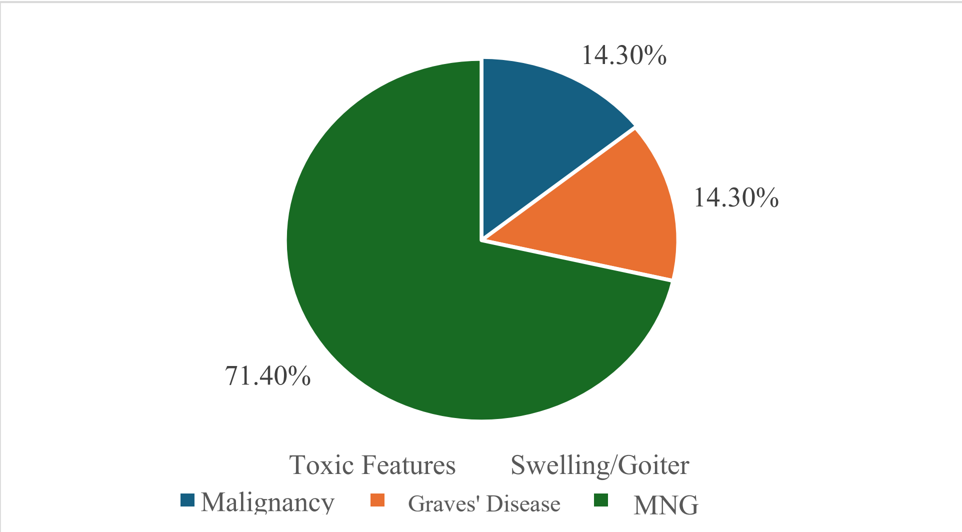


Chart 34:Preop indication and frequency of hypocalcemia

Table 19:Age group-Frequency of hypocalcemia

Age Group (yr)	Frequency	Percentage
18-30	0	0
30-45	3	21.4%
45-60	8	57.1%
>60	3	21.4%
Total	14	100%

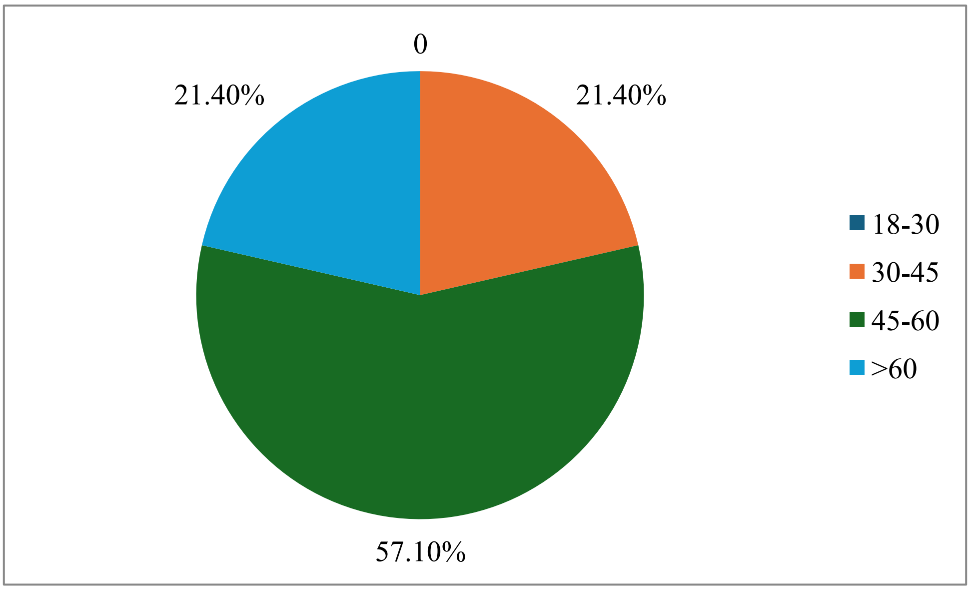


Chart 35:Age group and frequency of hypocalcemia

Age group and frequency of hypocalcemia Group 1; 0 patient
Group 2:3 patients
Group 3:8 patients
Group 4:3 patients

INCIDENCE OF HYPOCALCEMIA ON PROPORTION OF PATIENTS WHO DEVELOPED HYPOCALCEMIA ON DAY 2

Variable	Mean ± SD	Median (Q1, Q3)	Minimum	Maximum
SERUM CA	**8.13 ± 0.19**	**8.15 (8.00,8.30)**	**7.7**	**8.4**

Table 20:Manifested symptoms and frequency

Symptoms	Frequency	Percentage
Asymptomatic	3	21.4%
Carpopedal Spasm	1	7.1%
Finger Numbness	1	28.6%
Oral Numbness	6	42.9%
Total	14	100%

On post op day 2:3 asymptomatic,1 carpopedal spasm,1 finger numbness, oral numbness

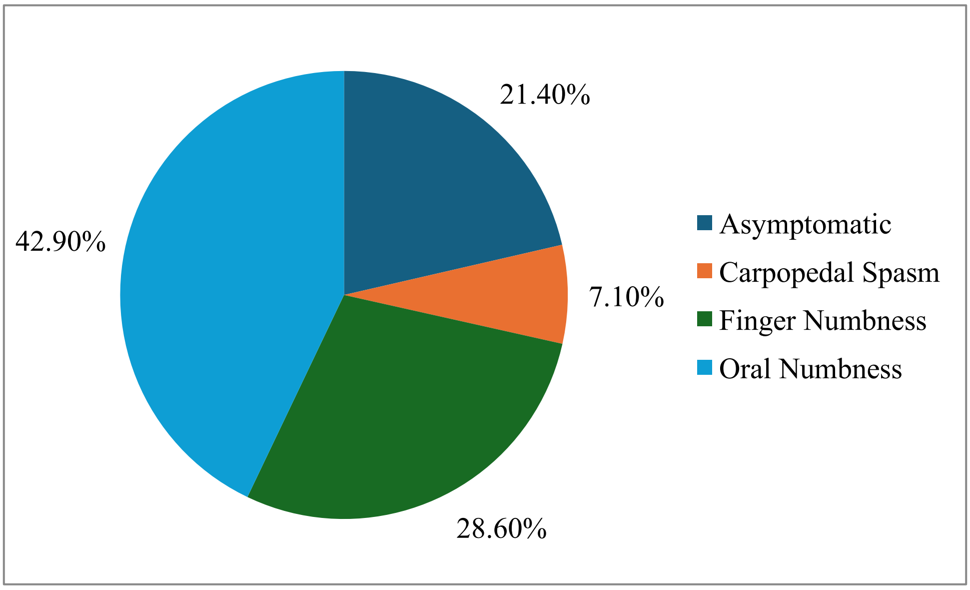


Chart 36:Manifested symptoms and frequency

Table 21:Gender and frequency

Gender	Frequency	Percentage
Male	1	7.1%
Female	13	92.9%
Total	14	100%

On post op day 2:1 male patient and 13 female

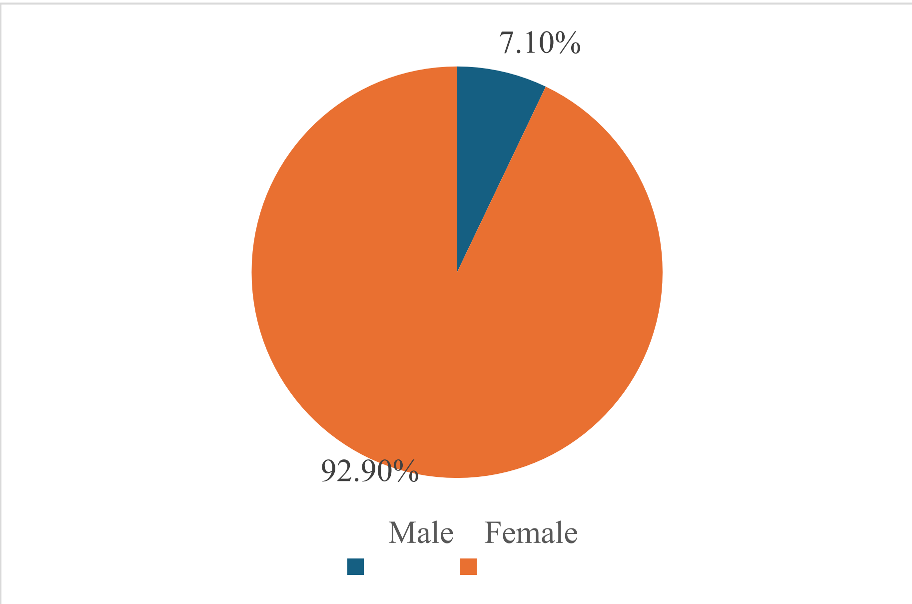


Chart 37:Gender and frequency

Table 22:Pre op indications and frequency of hypocalcemia

Preoperative Indications for Total Thyroidectomy	Frequency	Percentage
Malignancy	4	28.6%
Grave‘s disease	2	14.3%
MNG	8	57.1%
Total	14	100%

Pre op indication and frequency of hypocalcemia Malignancy 4, Grave‘s disease 2, MNG 8

Chart 38:Pre op indications and frequency of hypocalcemia

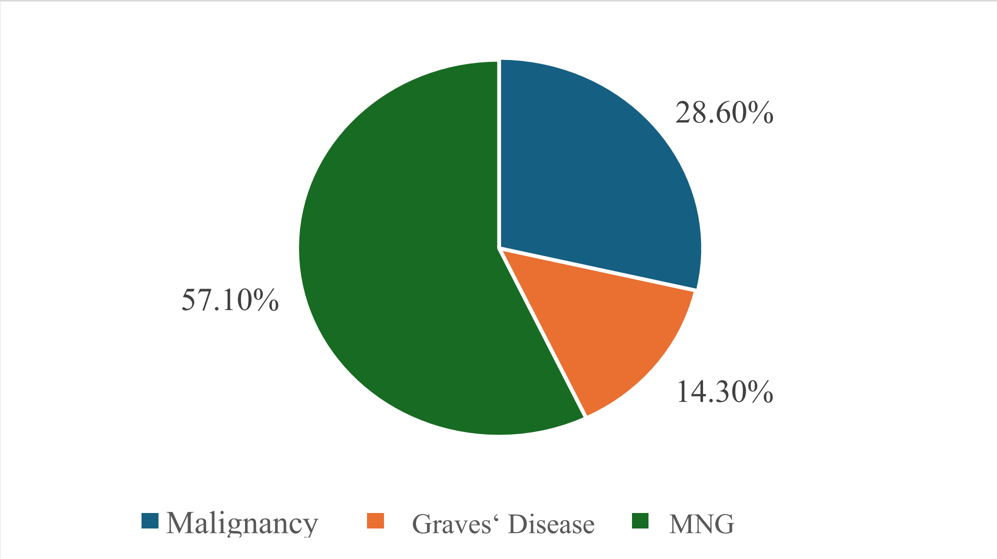


Table 23:Age group-frequency

Age Group (yr)	Frequency	Percentage
18-30	0	0
30-45	2	14.3%
45-60	8	57.1%
>60	4	28.6%
Total	14	100%

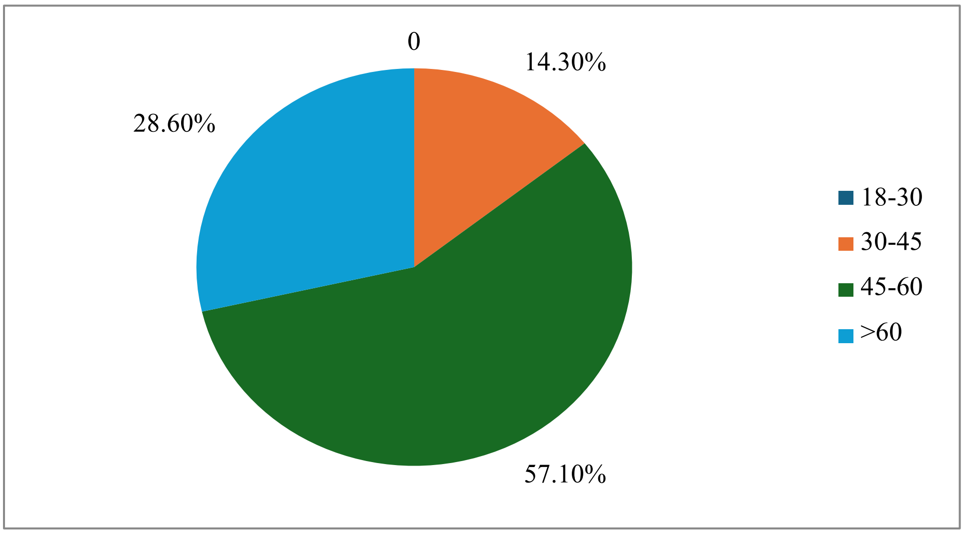


Chart 39:Age group-frequency

Age group and frequency of hypocalcemia Group 1:0 patient
Group 2:2 patients
Group 3:8 patients
Group 4:4 patients

PROPORTION OF PATIENTS WHO DEVELOPED HYPOCALCEMIA ON DAY 3

Variable	Mean ± SD	Median (Q1, Q3)	Minimum	Maximum
SERUM CA	8.32 ± 0.07	8.30 (8.3,8.4)	8.2	8.4

Table 24:Manifested symptoms and frequency

Symptoms	Frequency	Percentage
Asymptomatic	0	0
Carpopedal Spasm	1	12.5%
Finger Numbness	3	37.5%
Oral Numbness	4	50%
Total	8	100%

On post op day 3:0 asymptomatic,1 carpopedal spasm, 3 finger numbness,4 oral numbness

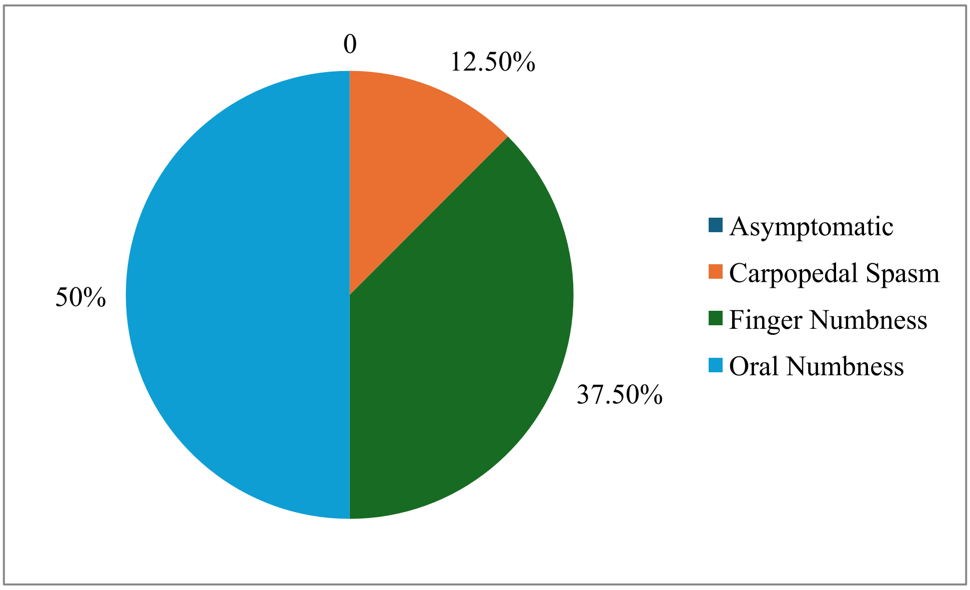


Chart 40:Manifested symptoms and frequency

Table 25:Gender-Frequency

Gender	Frequency	Percentage
Male	2	25%
Female	6	75%
Total	8	100%

On post op day 3:2 male patient and 6 male patient

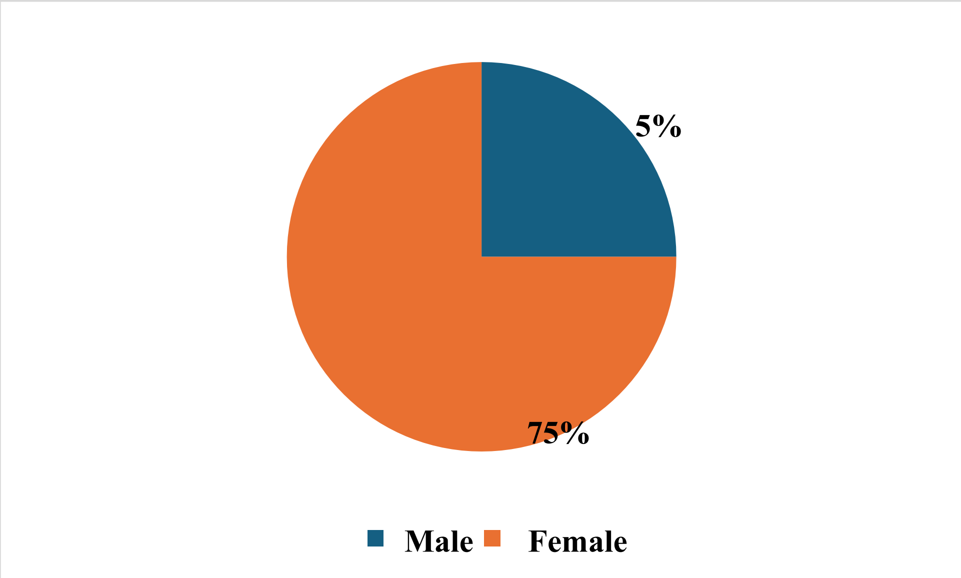


Chart 41:Gender –frequency

Table 26:Preop indications and frequency

Preoperative Indications for Total Thyroidectomy	Frequency	Percentage
Malignancy	3	37.5%
Grave's disease	1	12.5%
MNG	4	50%
Total	8	100%

Pre op indications and frequency of hypocalcemia Malignancy 3, Grave's disease 1, MNG 4

Table 27:Age group and frequency

Age Group (yr)	Frequency	Percentage
18-30	0	0
30-45	0	0
45-60	5	62.5%
>60	3	37.5%
Total	8	100%

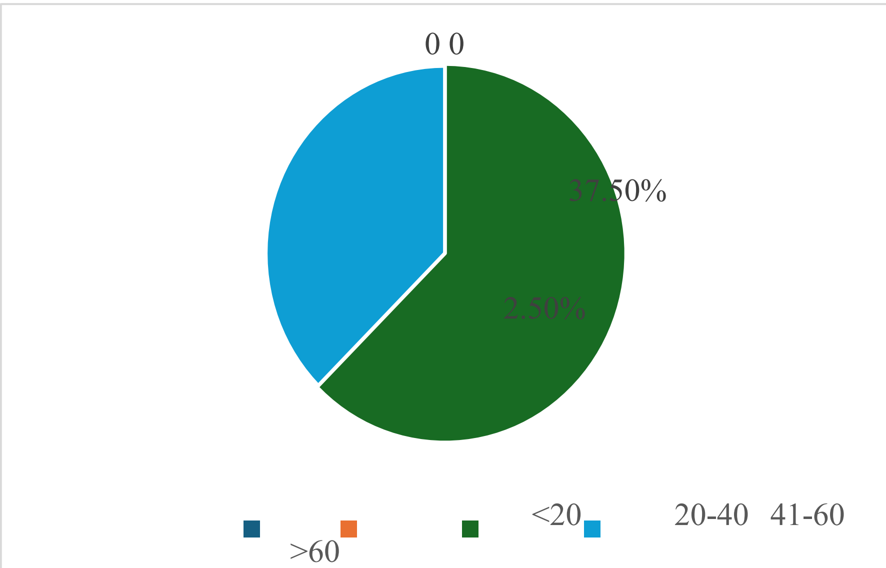


Chart 42:Age group and frequency

Age group and frequency of hypocalcemia

Group 1:0 patient	Group 2:0 patient
Group 3:5 patients	Group 4:patients

DISCUSSION

Thyroid disorder are most common endocrine gland diseases worldwide. Different diseases presentation like malignancy, thyroiditis, grave‘s disease, toxic MNG, multinodular goitre, hyperthyroidism, compressive symptoms are usually encountered in our daily practice. It can be either manage medically or by surgery. Even though thyroidectomy is common procedure and considered safe even in hands of experience surgeon complications like post thyroidectomy hypocalcemia, RLN injury, hematoma, seroma, stridor, hypothyroidism, infection, airway obstruction still persist.

Post operative hypocalcemia is one of the common complication and challenges facing by the surgeons. It‘s considered multifactorial risk factor parathyroid glands injury, age, sex, autoimmune, grave‘s disease, malignancy, extent of surgery, gland size, presence of fibrosis and inflammation, neck node dissection but most important factors being due to hypoparathyroidism caused by accidental removal of parathyroid glands or injury during surgery. Post thyroidectomy hypocalcemia can be transient or permanent. Preservation of parathyroid gland‘s during surgery requires accuracy, experience and good knowledge of anatomy of neck.

In our study results shows that Thyroid diseases are far more common in females than male as mention in many other literature. Our study 87.8% were female population. Similarly Post operative hypocalcemia found to be more common in female. Sands NB et al study shows that post operative hypocalcemia is 24.7% in female and 11.8% in male [13,38,39], Paolo Del Rio et al study shows female patients experienced postoperative hypocalcemia in 42% (701/1669) of cases, which was signicantly higher than the 21.4% (94/439) identified in men[3]

Even if Thyroidectomy is done in different age group post op hypocalcemia is more common with older or advance age group. In our study 62% were between 45-60years. Study conducted by Arumugam et al. (2017) reported post thyroidectomy hypocalcemia was more common in age more than 50 years. Erbil et. Al (2009) also documented hypcalcemia increases with advancing age.[43,44].

Post op thyroidectomy hypocalcemia incidence is 32.6% in our study and permanent hypocalcemia is 0%. In study conducted by Bezawada et al (2023) was 46.9% and permanent hypocalcemia 3.7% . Edafe et al (2014) study also reported temporary hypocalcemia following total thyroidectomy was 27 (19-28)% and permanent hypocalcemia was 0-3%[45,46]

In our study although MNG is maximum pre op indication for thyroidectomy the maximum post op hypocalcemia seen in malignancy 57%, Grave‘s disease followed by MNG. In other study like Arumugam et al (2017), Malinancy and grave‘s disease shows higher incidence of hypocalcemia probably due to larger extension of surgery [43,13].

we used serial post operative (POD 1, 2,3) serum calcium as predictor for hypocalcemia which shows on POD 1 and POD 2 hypocalcemia was found to be 29% each while on POD 3 found to be 16%. Patients undergoing total thyroidectomy needs serial monitoring of calcium to check and manage hypocalcemia. According to study conducted by Edafe et al study also suggest that incidence of hypocalcemia on POD 1 was 29%, subsequent day 35.3% and it is further suggest that incidence of hypocalcemia is underestimated by 6% only when POD 1 measurement was done[47]. However despite of delaying discharge or longer hospital stay and daily serum calcium monitoring other literature suggest PTH measurement intraoperative PTH or quick PTH assay [48] PTH 1hours after thyroidectomy[27] PTH 1and 24 hours [26,27,28] will shortly predicts chances of hypocalcemia and

normal PTH level can be safely discharge. However the cost factor and availability is the limiting factor.
Hypocalcemia leads to increased neuromuscular excitability and cardiac electrical instability, as it lowers the threshold for nerve and muscle cell depolarization. symptoms often include paresthesias, such as numbness and tingling around the mouth and fingertips. Muscle stiffness, cramps, and spasms are also common, neuropsychiatry symptoms like confusion, irritability, anger, depression, and light headedness. Signs of hypocalcemia chovstek, trousseau sign/carpopedal spasm.

In our study perioral numbness constitute 44%, finger numbness 31%, carpopedal spasm 6% and asymptomatic 19%. Manifestation of this required timely recognition, intervention with calcium supplementation (oral/iv), serial serum calcium estimation and education of patient [12,13,14,19,20,21,43]

During thyroidectomy injury to parathyroid or devascularization of gland is important significant factor of hypocalcemia and therefore to improve the outcome after parathyroid gland injury simultaneous autotransplantation is recommended. In our study in two patients autotransplantation of parathyroid is done and post operatively no hypocacemia was found [4]. And due to advancememt in Thyroidectomy certain techniques like methylene blue spray showed sensitivity of 98.46%, specificity 97.01%, NPV of 98.4% highlighting reliability in ruling out their presence and overall accuracy of 97.73% proving that methylene blue spray as effective, precise and reliable method of parathyroid identification and reducing complication[48]. Sherif Monib et al study also mentioned that with methylene blue spray parathyroid gland identification is 82% (41/50 patients) with no significant hypocalcemia[49]

LIMITATIONS

- Sample size of the study was low, study would have been better with more sample size.
- Serum calcium monitoring not only the exclusive predictors of hypocalcemia.
- Difficult follow up for some patients.

CONCLUSION

Inthe present study ―CLINICAL EVALUATION OF HYPOCALCEMIA AFTER THYROIDECTOMY‖ it can be concluded that the incidence of hypocalcemia is 32.6% with more incidence found in older age, malignant lesion, Grave‘s disease, female sex. Parathyroid glands identification and preservation plays key role in post thyroidectomy hypocalcemia.

SUMMARY

From our study we bring the conclusion that post thyroidectomy transient hypocalcemia is a frequent common complication.
Proper anatomy of the gland, identification, preservation and meticulous dissection of parathyroid gland is the key. Along with that serial post op monitoring of serum calcium and recognition of hypocalcemia signs and symptom, supplementation of calcium if necessary, patient education can prevent the morbidity fom hypocalcemia.

Thyroid diseases are more common in female.

For doing Thyroidectomy in older age group surgeon should kept in mind regarding more chances of hypocalcemia with ages, toxicity and malignant lesion.

For smaller sector and considering cost effective serial monitoring of calcium, monitoring of signs and symptoms of hypocalcemia, educating patient of symptoms is efficient and acceptable to manage post op hypocalcemia.

REFERENCES

1. SriVignesh, M., Arun, A. M., & Robinson, S. R. (2023). Prevalence and Outcome of Post-thyroidectomy Hypocalcaemia: A Prospective Clinical Study. British Journal of Healthcare and Medical Research, 10(1). 1-13. DOI:10.14738/jbemi.101.1363 [1]
2. Alqahtani SM, Alatawi AS, Alalawi YS. Post-Thyroidectomy Hypocalcemia: A Single-Center Experience. Cureus. 2021 Nov 29;13(11):e20006. doi: 10.7759/cureus.20006. PMID: 34987897; PMCID: PMC8716130.[2]
3. Del Rio P, Rossini M, Montana CM, Viani L, Pedrazzi G, Loderer T, Cozzani F. Postoperative hypocalcemia: analysis of factors influencing early hypocalcemia development following thyroid surgery. BMC Surg. 2019 Apr 24;18(Suppl 1):25. doi: 10.1186/s12893-019-0483-y. PMID: 31074401; PMCID: PMC7402573.[3]
4. Kim YS. Impact of preserving the parathyroid glands on hypocalcemia after total thyroidectomy with neck dissection. J Korean Surg Soc. 2012 Aug;83(2):75-82. doi: 10.4174/jkss.2012.83.2.75. Epub 2012 Jul 25. PMID: 22880180; PMCID: PMC3412187.[4]
5. GRAY'S Anatomy 42 edition page 285 [5]
6. Allen E, Fingeret A. Anatomy, Head and Neck, Thyroid. 2023 Jul 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29262169. [6]
7. Bhargav PR. Salient anatomical landmarks of thyroid and their practical significance in thyroid surgery: a pictorial review of thyroid surgical anatomy (revisited). Indian J Surg. 2014 Jun;76(3):207-11. doi: 10.1007/s12262-013-0856-x. Epub 2013 Jan 27. PMID: 25177118; PMCID: PMC4141060. [7]
8. Yalçin B, Poyrazoglu Y, Ozan H. Relationship between Zuckerkandl's tubercle and the inferior laryngeal nerve including the laryngeal branches. Surg Today.2007;37(2):109-13. doi: 10.1007/s00595-006-3346-y. Epub 2007 Jan 25. PMID: 17243027. [8]
9. Ilahi A, Muco E, Ilahi TB. Anatomy, Head and Neck, Parathyroid. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30725888. [9]
10. Ganong physiology 26th edition page 369-382[10]
11. Guyton and Hall Textbook of medical physiology 14th edition page 991-1004 [11]
12. HARRISON'S principles of internal medicine 21st edition page 3160, 3185 [12]
13. Sinha V, Chaudhari NP, Jha SG, Parmar BD, Patel RS, Dave GP. Post- Thyroidectomy Hypocalcemia: Clinical Study at Tertiary Care Center. Indian J Otolaryngol Head Neck Surg. 2022 Oct;74(Suppl 2):2076-2081. doi: 10.1007/s12070-020-02023-4. Epub 2020 Aug 3. PMID: 36452542; PMCID: PMC9702187.[13]
14. Orloff LA, Wiseman SM, Bernet VJ, Fahey TJ 3rd, Shaha AR, Shindo ML, Snyder SK, Stack BC Jr, Sunwoo JB, Wang MB. American Thyroid Association Statement on Postoperative Hypoparathyroidism: Diagnosis, Prevention, and Management in Adults. Thyroid. 2018 Jul;28(7):830-841. doi: 10.1089/thy.2017.0309. Epub 2018 Jun 29. PMID: 29848235. [14]
15. SABISTON TEXTBOOK of SURGERY 21st edition Page 910-916 [15]
16. Bailey and love's SHORT PRACTICE OF SURGERY 28th edition Page 863- 866 [16]
17. Bliss RD, Gauger PG, Delbridge LW. Surgeon's approach to the thyroid gland: surgical anatomy and the importance of technique. World J Surg. 2000 Aug;24(8):891-7. doi: 10.1007/s002680010173. PMID: 10865032. [17]
18. Liang JJ, Irizarry R, Victor LS, Hoepner LA, Chernichenko N. Postoperative Complications After Total Thyroidectomy for Patients With Graves' Disease. Otolaryngol Head Neck Surg. 2023 Apr;168(4):754-760. doi: 10.1177/01945998221108050. Epub 2023 Jan 27. PMID: 35763358. [18]
19. Ancuta Leahu, Vanessa carroni, G.Bilotti, calcium level, a pedictive factor of hypocalcemia following total thyroidectomy, Jurnalul Chirurgie ,lasi, 2009, Vol5.Nr.2 (ISSN 1584-9341)[19]
20. Nahas ZS, Farrag TY, Lin FR, Belin RM, Tufano RP. A safe and cost-effective short hospital stay protocol to identify patients at low risk for the development of significant hypocalcemia after total thyroidectomy. Laryngoscope. 2006 Jun;116(6):906-10. doi: 10.1097/01.mlg.0000217536.83395.37. PMID: 16735895. [20]

21. Graff AT, Miller FR, Roehm CE, Prihoda TJ. Predicting hypocalcemia after total thyroidectomy: parathyroid hormone level vs. serial calcium levels. Ear Nose Throat J. 2010 Sep;89(9):462-5. PMID: 20859873.[21]
22. Sonkhya N, Agarwal S, Choudhary MP, Gupta N. Serial Estimation of Serum Calcium and Ionic Calcium Level for Early Detection of Hypocalcemia After Total/Completion Thyroidectomy. Indian J Otolaryngol Head Neck Surg. 2023 Dec;75(4):3493-3496. doi: 10.1007/s12070-023-04031-6. Epub 2023 Jul 1. PMID: 37974829; PMCID: PMC10645760. [22]
23. Al Maawali H, Al Badaai Y. Serum calcium relative decline as a predictor of post thyroidectomy hypocalcaemia. J Laryngol Otol. 2025 Feb;139(2):125-128. doi: 10.1017/S0022215124001270. Epub 2024 Oct 22. PMID: 39435505. [23]
24. Walsh SR, Kumar B, Coveney EC. Serum calcium slope predicts hypocalcaemia following thyroid surgery. Int J Surg. 2007 Feb;5(1):41-4. doi: 10.1016/j.ijsu.2006.03.006. Epub 2006 May 23. PMID: 17386914. [24]
25. Lee YH, Liu Z, Zheng L, Qiu J, Sang J, Guan W. The Rate of Postoperative Decline in Parathyroid Hormone Levels Can Predict Symptomatic Hypocalcemia Following Thyroid Cancer Surgery with Neck Lymph Node Dissection. Nutr Cancer. 2025;77(1):1-8. doi: 10.1080/01635581.2024.2401179. Epub 2024 Sep 23. PMID: 39313935. [25]
26. Lam A, Kerr PD. Parathyroid hormone: an early predictor of postthyroidectomy hypocalcemia. Laryngoscope. 2003 Dec;113(12):2196-200. doi: 10.1097/00005537-200312000-00029. PMID: 14660927. [26]
27. AlQahtani A, Parsyan A, Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia. Can J Surg. 2014 Aug;57(4):237-40. doi: 10.1503/cjs.008013. PMID: 25078927; PMCID: PMC4119114. [27]
28. Soon PS, Magarey CJ, Campbell P, Jalaludin B. Serum intact parathyroid hormone as a predictor of hypocalcaemia after total thyroidectomy. ANZ J Surg. 2005 Nov;75(11):977-80. doi: 10.1111/j.1445-2197.2005.03593.x. PMID: 16336392. [28]
29. Semanate F, Tarupi W, Fernandez Trokhimtchouk T, Palacios C, Jaramillo O. The Role of Parathyroid Hormone Level as a Predictor of Hypocalcemia After Total Thyroidectomy for Thyroid Cancer: A Cross-Sectional Study. Cureus. 2025 Feb 12;17(2):e78897. doi: 10.7759/cureus.78897. PMID: 40091995; PMCID: PMC11908629.[29]
30. Maheshwari M, Khan IA. Risk Factors for Transient and Permanent Hypoparathyroidism Following Thyroidectomy: A Comprehensive Review. Cureus. 2024 Aug 9;16(8):e66551. doi: 10.7759/cureus.66551. PMID: 39258042; PMCID: PMC11383864.[30]
31. Trupka A, Sienel W. Simultane Autotransplantation von Nebenschilddrüsengewebe im Rahmen der totalen Thyreoidektomie
32. parathyroid gland during thyroidectomy in benign thyroid disease minimizes the risk of permanent hypoparathyroidism]. Zentralbl Chir. 2002 May;127(5):439-42. German. doi: 10.1055/s-2002-31974. PMID: 12058305.
33. Barczyński M, Gołkowski F, Nawrot I. Parathyroid transplantation in thyroid surgery. Gland Surg. 2017 Oct;6(5):530-536. doi: 10.21037/gs.2017.06.07. PMID: 29142845; PMCID: PMC5676165.[32]
34. Lahey FH. The transplantation of parathyroids in partial thyroidectomy. Surg Gynecol Obstet. 1926;62:508–9. [33]
35. Zedenius J, Wadstrom C, Delbridge L. Routine autotransplantation of at least one parathyroid gland during total thyroidectomy may reduce permanent hypoparathyroidism to zero. Aust N Z J Surg. 1999 Nov;69(11):794-7. doi: 10.1046/j.1440-1622.1999.01697.x. PMID: 10553968. [34]
36. Lo CY. Parathyroid autotransplantation during thyroidectomy. ANZ J Surg. 2002 Dec;72(12):902-7. doi: 10.1046/j.1445-2197.2002.02580.x. PMID: 12485231. [35]
37. Olson JA Jr, DeBenedetti MK, Baumann DS, Wells SA Jr. Parathyroid autotransplantation during thyroidectomy. Results of long-term follow-up. Ann Surg. 1996 May;223(5):472-8; discussion 478-80. doi: 10.1097/00000658- 199605000-00003. PMID: 8651738; PMCID: PMC1235165. [36]

38. Calcium as a predictor of hypocalcemic symptoms post total thyroidectomy. Osteoporos Int. 2019 Dec;30(12):2495-2504. doi: 10.1007/s00198-019-05040-4. Epub 2019 Aug 28. PMID: 31463588.[37]
39. Sands NB, Payne RJ, Côté V, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. Otolaryngol Head Neck Surg. 2011 Oct;145(4):561-4. doi: 10.1177/0194599811414511. Epub 2011 Jul 12. PMID: 21750342.[38]
40. Ozogul B, Akcay MN, Akcay G, Bulut OH. Factors affecting hypocalcaemia following total thyroidectomy: a prospective study. Eurasian J Med. 2014 Feb;46(1):15-21. doi: 10.5152/eajm.2014.03. PMID: 25610288; PMCID: PMC4261442.[39]
41. Hosseini M, Otaghvar HA, Tizmaghz A, Shabestanipour G, Vahid PA. Evaluating the Time Interval for Presenting the Signs of Hypocalcaemia after Thyroidectomy. J Clin Diagn Res. 2016 Mar;10(3):PC19-22. doi: 10.7860/JCDR/2016/15274.7445. Epub 2016 Mar 1. PMID: 27134928; PMCID: PMC4843313.[40]
42. Mitra I, Nichani JR, Yap B, Homer JJ. Effect of central compartment neck dissection on hypocalcaemia incidence after total thyroidectomy for carcinoma. J Laryngol Otol. 2011 May;125(5):497-501. doi: 10.1017/S0022215110002471. Epub 2010 Nov 25. PMID: 21106140.[41]
43. Shuchleib-Cung A, Garcia-Gordillo JA, Ferreira-Hermosillo A, Mercado M. Risk factors for hypocalcemia after total thyroidectomy. Cir Cir. 2022;90(6):765- 769. English. doi: 10.24875/CIRU.21000579. PMID: 36472864.[42]
44. Arumugam S, Mohankumar A, Muthukumaraswamy A, Anandan H (2017) Clinical study of Hypocalcemia following Thyroid Surgery. International Journal of Scientific Study,4(11):37-41 [43]
45. Erbil Y, Barbaros U, Temel B, Turkoglu U, Issever H, Bozbora A, et al (2009).The impact of age, vitamin D3 level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. Am J Surg, 197:439-46 [44]
46. Ramakrishna Bezawada, Narendra MC, Mutheeswaraiah Y, Rukmangadha N. (2023).The Incidence of Hypocalcemia following Total Thyroidectomy: A Retrospective Study. SVU-International Journal of Medical Sciences. Vol.6, Issue 1, pp:457-464 [45]
47. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. (2014). Systematic review and metanalysis of predictors of post thyroidectomy hypocalcemia, Br J Surg.101(4):307-20 [46]
48. Edafe O, Prasad P, Harrison BJ, Balasubramanian SP. Incidence and predictors of post-thyroidectomy hypocalcaemia in a tertiary endocrine surgical unit. Ann R Coll Surg Engl. 2014 Apr; 96 (3):219-23. doi: 10.1308/003588414X13814021679753. PMID: 24780788; PMCID: PMC4474053.[47]
49. Lo CY, Luk JM, Tam SC. Applicability of intraoperative parathyroid hormone assay during thyroidectomy. Ann Surg. 2002 Nov;236(5):564-9. doi: 10.1097/00000658-200211000-00005. PMID: 12409661; PMCID: PMC1422613.[48]
48. Ballal N, Kotennavar MS, Patil AV, Rajendra B, Jaju P, Savant MS, Rathod SS, Ghanteppagol V, Shetty S, Medikonda E. Methylene Blue Spray as a Tool for Safe Thyroidectomy. Cureus. 2024 Nov 15;16(11):e73790. doi: 10.7759/cureus.73790. PMID: 39687816; PMCID: PMC11647191.[48]
49. Monib S, Mohamed A, Abdelaziz MI. Methylene Blue Spray for Identification of Parathyroid Glands During Thyroidectomy. Cureus. 2020 Nov 19;12(11):e11569. doi: 10.7759/cureus.11569. PMID: 33364096; PMCID: P