EARLY POSTOPERATIVE COMPLICATIONS OF THYOIDECTOMY AT THE MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

MULANDA GILBERT MUSASIA

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MOI UNIVERSITY, SCHOOL OF MEDICINE

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university. No part of this thesis may be reproduced without prior written permission of the author and or Moi University.

MULANDA GILBERT MUSASIA

SM/PGGS/02/11

SIGN …… **DATE ……**

Declaration by supervisors

This thesis has been submitted with our approval as university supervisors.

DR. G. JUMBI
Consultant General Surgeon and Senior Lecturer
Department of Surgery and Orthopedics
Kenyatta University, School of Health Sciences, Nairobi

SIGN: …… **DATE: ……..**

DR. R. SHITSINZI
Consultant Anesthesiologist
Department of Surgery and Anesthesiology
Moi University, School of Medicine, Eldoret

SIGN: …….. **DATE: …….**

DEDICATION

This work is dedicated to my Father, Amadalo and my Mother, Rosila for illuminating the path ever so brightly, and to my grandmother, Zillah for a foundation well laid. Last but not least, to my wife Kendy, for all the support provided.

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ABSTRACT

BACKGROUND: Complications arising from thyroidectomy can be life threatening and the morbidity, lifelong. The complication rate, a sensitive measure of the quality of surgery, varies from center to center. This study aims to quantify and characterize these complications at MTRH.

OBJECTIVE: To investigate the spectrum and distribution of early postoperative complications of thyroidectomy and their determinant factors.

METHODOLOGY: *Study design*: observational, cross sectional. *Sampling technique*: Consecutive purposive. *Sample size:* 74 patients. *Study Site*: MTRH general surgery outpatient clinics, inpatient wards and operating theatres. *Study period*: August 2012 – July 2013. *Eligibility*: goitre patients with an indication for thyroidectomy. *Exclusion*: prior neck irradiation, neck dissection. *Study variables*: Patient demographics, goitre characteristics, surgery indications, extent of surgery and intraoperative observations were analyzed as determinant factors. *Study tool*: Interviewer administered questionnaire. *Analysis*: Contingency tables with Fischer's exact and Student's t-tests used to evaluate association between complications and multiple determinant factors. Statistical significance set at p-value <0.05.

RESULTS: There were 73 females and 1 male recruited into the study with mean±SD age of 49.54±12.584 years**.** Overall complication rate was 33.8% (n = 25). This corresponded to 9 (12.2%) hypoparathyroidism, 4 (5.4%) laryngeal nerve palsies, 2 (2.7%) hematomas, 5 (6.8%) flap oedema, 3 (4.1%) surgical site infections, 6 (8.1%) seromas and 3 (4.1%) airway obstructions. Significant determinant factors were extent of resection (p=<0.001), FNAC malignancy (p=0.026), FNAC thyroiditis (p=0.007). Older age was associated with higher risk of wound infection (p=0.001). Most goitres were WHO grades II and III, benign and non-toxic.

CONCLUSIONS: Early post-thyroidectomy complications are common. Hypoparathyroidism is the most frequent. Extent of resection is the main determinant factor.

RECOMMENDATIONS: Surgeons should have a high threshold for performing extensive resections. Consider adopting established global perioperative protocols for thyroid surgery that include routine parathyroid gland auto-transplantation in extensive resections.

Contents

DECLARATION i
DEDICATION ii
ACKNOWLEDGEMENT viii
DISCLOSURE ix
ABBREVIATIONS AND ACRONYMS x
DEFINITION OF TERMS xi
1 INTRODUCTION 1
1.1 Background 1
1.2 Problem statement 3
1.3 Justification 3
1.4 Research Question 3
1.5 Study objectives 4
1.5.1 Broad Objective 4
1.5.2 Specific objectives 4
2 Literature Review 5
2.1 Introduction 5
2.2 Anatomy and Physiology of the thyroid Gland 9
2.3 Preoperative evaluation of goitres 12
2.4 Indications of Thyroidectomy 17
2.5 Contraindications to thyroidectomy 20
2.6 Standard thyroidectomy procedure (Conventional Thyroidectomy) 21
2.7 Minimally invasive thyroidectomy (MAT, MIVAT) 23
2.8 Postoperative complications and their determinants 25
2.8.1 Hypocalcaemia 26
2.8.2 Recurrent laryngeal nerve injury 30
2.8.3 Postoperative bleeding 32
2.8.4 Airway Obstruction 34
2.8.5 Post-operative Hypothyroidism 35
2.8.6 Seroma formation 36
2.8.7 Surgical site infection 37
2.8.8 Flap edema 38

2.8.9 Thyroid Crisis 39
3 Methodology 41
3.1 Introduction 41
3.2 Study setting 41
3.3 Study population 42
3.4 Sampling procedure 44
3.5 Study design 45
3.6 Study Methods 45
3.7 Data processing and Analysis 50
3.8 Study limitations 50
3.9 Ethical considerations 51
4 Results 53
4.1 Demographic characteristics 53
4.2 Goitre characteristics 55
4.3 Indications for surgery 62
4.4 Early postoperative complications 62
4.4.1 Factors determining complications (Hypothesized causal variables) 62
4.4.2 Early postoperative complications and their determinants 66
4.4.3 Overall complication and the extent of thyroidectomy 79
4.4.4 Summary of complications and their determinants 81
5 Discussion 83
5.1 Demographics 83
5.2 Goitre characteristics 84
5.3 Clinical observations 87
5.4 Early Complications of thyroidectomy 89
6 Conclusions and Recommendations 99
6.1 Conclusions 99
6.2 Recommendations 100
References 101
7 Appendix I: CONSENT FORM 117
APPENDIX II: QUESTIONNAIRE 118
Appendix III: IREC approval 124

Appendix IV: MTRH Approval 125

LIST OF TABLES

Table 1: The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management 15
Table 2: Thyroid Pathology 16
Table 3: Tribal constitution of patients with goitres 54
Table 4: Geographical areas of residence of patients with goitres 54
Table 5: Preoperative clinical diagnoses 55
Table 6: Preoperative FNAC diagnoses 57
Table 7: Histological diagnosis of patients with goitre 58
Table 8: Comparison of FNAC versus Histology 59
Table 9: Sensitivity of FNAC 60
Table 10: Effect of FNAC diagnosis on the extent of surgery 61
Table 11: Indications for Surgery 62
Table 12: Surgeon specialisation 63
Table 13: Type/extent of thyroidectomy procedures 64
Table 14: Clinical summary 65
Table 15: Technique/type of dissection analysed by surgeon 66
Table 16: Variables associated with postoperative Laryngeal nerve injury: Bivariate analysis. 68
Table 17: Postoperative Serum calcium levels 70
Table 18: Assessment of postoperative hypocalcemia by Chvostek's test 70
Table 19: Assessment of postoperative hypocalcemia by Trousseau's sign 70
Table 20: **Variables associated with postoperative Hypocalcemia: Bivariate analysis** 72
Table 21: Summary of two patients with postoperative bleeding 73
Table 22: Variables associated with "significant" postoperative postop bleeding 74
Table 23: Variables associated with postoperative seroma: Bivariate analysis 76
Table 24: Variables associated with surgical site infection: Bivariate analysis 77
Table 25: Presence of flap oedema 78
Table 26: Association between extent of surgery and overall complication 79
Table 27: Association between surgeon and overall complication 79
Table 28: Analysis of early postoperative complications by extent of surgery. 80
Table 29: Variables associated with postoperative complication: Bivariate analysis 82

LIST OF FIGURES

Figure 1: Enrolment Schema 45
Figure 2: Age distribution of patients who underwent thyroidectomy 53
Figure 3: Preoperative Thyroid Function Tests 56
Figure 4:Hypocalcemia – patient flow 69

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The investigator did not receive any outside funding or grants in support for this study. Neither he nor a member of his immediate family received payments or other benefits or commitment or agreement to provide such benefits from a commercial entity.

Sign……

Date……

Mulanda Gilbert Musasia

SM/PGGS/02/11

ABBREVIATIONS AND ACRONYMS

CT – Conventional Thyroidectomy

FNA – Fine Needle Aspiration

FNAC – Fine Needle Aspiration Cytology

Hb – Hemoglobin Levels

IREC – Institutional Research and Ethics Committee

MIT – Minimally Invasive Thyroidectomy

MIVAT – Minimally Invasive Video Assisted Thyroidectomy

MTRH – Moi Teaching and Referral Hospital

OPD – Outpatient Department

PACU – Post Anesthesia Care Unit

RLN – Recurrent Laryngeal Nerve

SLN – Superior Laryngeal Nerve

SPSS – Statistical Packages for Social Sciences

SSI – Surgical Site Infection

TFT – Thyroid Function Tests

U/S – Ultrasonography

WBC – White Blood Cell Count

WHO – World Health Organization

ENT – Ear Nose Throat

CT scan – Computed tomographic scan

FDG-PET – Fluorodeoxyglucose Positron Emission Tomography

DEFINITION OF TERMS

Early Postoperative complication: This referred to complications arising within a period of up to six weeks postoperatively. Six weeks' time interval was chosen based on the fact that most transient, and confounding, postoperative clinical-pathological observations resolve by this time (Acun et al., 2004; Jessie & Harrison, 2010; Wahome, 2007). Examples of such observations include: "non-surgical" hypocalcaemia due to hemodilution and calcitonin release secondary to thyroid gland handling; voice changes due to glottic swelling, inflammation and laryngeal trauma during intubation.

Goitre – the abnormal enlargement of the thyroid gland

Thyroidectomy – complete or partial removal of the thyroid gland

Total Lobectomy – Removal of one thyroid lobe (with or without the isthmus)

Isthmusectomy – excision of the mid portion (isthmus) of the thyroid gland

Subtotal lobectomy – Partial removal of one thyroid lobe leaving about 4g of tissue.

Total thyroidectomy – bilateral total lobectomy + Isthmusectomy.

Subtotal thyroidectomy – bilateral subtotal lobectomy + Isthmusectomy. Aims to leave one-eighth of the total mass (approximately 4-5g) of thyroid tissue on each side

Near total thyroidectomy – removal of nearly all of each thyroid lobe leaving unresected only one-gram sleeve of thyroid tissue around the parathyroid glands and the recurrent laryngeal nerve's entrance into the larynx.

Hartley - Dunhill procedure – Total lobectomy on one side + Isthmusectomy + subtotal lobectomy on the contralateral side.

Hemi thyroidectomy – Total lobectomy on one side + Isthmusectomy

Extensive resection – Near total or Total thyroidectomies

Plummer's disease – toxic multinodular goitre

Grave's disease – autoimmune mediated diffuse toxic goitre

Chvostek–Weiss sign/test – Contraction of ipsilateral facial muscles elicited by tapping over the facial nerve as it courses between the zygomatic arch and the angle of the jaw just anterior to the ear (Cooper & Gittoes, 2008). The response ranges from twitching of the lips to spasm of all facial muscles and depends on the severity of hypocalcemia. This phenomenon is observed in 10 – 15% of normal subjects making this test a poor discriminator of patients with hypocalcaemia.

Trousseau's sign – the induction of carpopedal spasm by inflation of a sphygmomanometer above systolic pressure for three minutes (Cooper & Gittoes, 2008; Thakker, 2006). Spasms are characterized by adduction of the thumb, flexion of the metacarpophalangeal joints, extension of the interphalangeal joints, and flexion of the wrist. May also be induced by voluntary hyperventilation for one to two minutes after cuff release.

Depends on effect of ischemia to increase excitability of the nerve trunk under the cuff, rather than the motor end plate; excitability is maximal at three minutes and returns to normal even if ischemia is maintained longer. This sign is 94% specific for hypocalcemia and is only found in 1% of normocalcaemic patients (Urbano, 2000).

Tracheomalacia - Softening of the cartilages of the trachea from longstanding pressure with subsequent narrowing with the negative inspiratory force of inhalation.(Singh, Lucente, & Shaha, 1994)

Registrar/Resident – A Medical Officer undergoing postgraduate training.

1 INTRODUCTION

1.1 Background

The highlands of Kenya's central, south-central Rift and western regions were traditionally regarded as being part of the endemic goitre belt of Eastern Africa.(Hanegraaf & McGill, 1970; Kelly & Snedden, 1958). Ecologically, these were areas where the soil had a low iodine content owing to prior glaciation. This resulted in poor iodine nutrition in the populace (Davies, 1994). Evidence shows that in the early stages of iodine deficiency, the thyroid gland adjusts by undergoing diffuse hyperplasia. Chronic iodine deficiency, on the other hand, leads to nodular hyperplasia, increased colloid content and increased height of follicular cells (Studer & Derwahl, 1995). Consequently, these areas had a high prevalence of nodular goitres and thyroid autonomy and thyroidectomy was a common elective surgical procedure (Karamanakos et al., 2010). Currently, thyroidectomy constitutes about 10% of the elective theatre case load at MTRH.

Generally, the indications for thyroidectomy include: patients with goitres accompanied by pressure manifestations on the trachea, esophagus, recurrent laryngeal nerves and the great neck veins; failed medical management of toxic goitres; cosmetic concerns and any clinical suspicion of malignant neoplasia(Goncalves Filho & Kowalski, 2005; Peiris & Peiris, 2006). Although thyroidectomy does achieve rapid symptomatic relief, it has the disadvantages of postoperative mortality, morbidity and the recurrence of goitre(Lando, Hoover, & Zuckerbraun, 1990). Surgeons therefore, strive to choose operations that will result in the least recurrence and lowest complication rates (Acun et al., 2004).

As per reported incidence rates, the major early postoperative complications of thyroidectomy are: recurrent laryngeal nerve palsy/injury (RLNP), hypoparathyroidism and postoperative hematoma (McHenry, 2002). Other minor, less frequent, complications include: surgical site infections, seroma, flap edema, hypothyroidism, upper airway obstruction and thyrotoxic crisis. Gradual improvements in surgical technique and instrumentation, anesthesia and methods of asepsis over the last century have led to a dramatic decline in the observed rates of these complications. Currently, mortality rates of less than 0.5% and morbidity rates of less than 3% are the globally acceptable standard (Bergamaschi, Becouarn, Ronceray, & Arnaud, 1998). Although rare, these complications can have potentially life threatening consequences (Idris, Ali, & Hamza, 2013).

The outcome and complication rates of thyroidectomy has been shown to be dependent on: surgeon skill and experience; extent of surgery; indication of surgery and the patient volume at that particular center (McHenry, 2002). As such, complication rates will vary from center to center. As an illustration, the complication rates reported in regional studies are five times higher than global standards i.e. mortality and morbidity rates of 0.5%–3.4% and 4.1%–14.6% respectively (Abebe, Girmaye, Mensur, Sentayehu, & Sissay, 2007; Chalya et al., 2011; Hill, Mwangi, & Wagana, 2004). This may have implications on the quality of surgery being offered locally.

The aim of this study was to evaluate the incidence and the risk factors for complications in patients undergoing thyroidectomy at MTRH.

1.2 Problem statement

The Moi Teaching and Referral Hospital serves a region traditionally considered to be endemic for goitre. As such, thyroidectomy is a common elective procedure. Regional studies show that the postoperative complications are higher than global standards. This may imply a lower quality of surgery. Furthermore, the associated determinant factors are not known. This might frustrate efforts at quality improvement.

1.3 Justification

This study will determine the complication rate of thyroidectomy at MTRH. This information will facilitate an assessment of the quality of surgery and enable both internal and external audits. In addition, the study will elicit the associated determinant factors. Addressing these factors will hopefully reduce the rate of complications and ultimately improve the quality and safety of thyroidectomy.

This study is also meant to act as a baseline study that will generate hypotheses that can be investigated in more rigorous analytical designs.

1.4 Research Question

What are the early post-operative complications of thyroidectomy at Moi Teaching and Referral Hospital?

1.5 Study objectives

1.5.1 Broad Objective

To investigate the spectrum and distribution of early postoperative complications of thyroidectomy and their determinant factors at MTRH.

1.5.2 Specific objectives

1. To determine the demographic features of patients with goitres presenting for thyroidectomy at MTRH.
2. To determine the goitre characteristics in patients undergoing thyroidectomy at MTRH.
3. To determine the early post-operative complications after thyroidectomy at MTRH.
4. To elicit the determinant factors of early post-operative complications of thyroidectomy at MTRH.

2 Literature Review

2.1 Introduction

This chapter cites literature at the international, regional and national levels. It focuses on the historical background of thyroidectomy, determinants of early postoperative complications, basic science (anatomy and physiology) of the thyroid gland, standard surgical procedure for thyroidectomy and the newest surgical techniques.

Historical background

Goitres (from the Latin word *guttur* for throat) have been known since 2700 B.C., long before the thyroid gland was recognized. The thyroid gland was first documented by the Italians of the Renaissance period. Leonardo da Vinci originally depicted the thyroid in his drawings as two separate glands on either side of the larynx in 1511 **(Leonardo, 1983)**. The term thyroid gland (Greek *thyreoeides*, shield-shaped) is attributed to Thomas Wharton in his Adenographia (1656). Although Bartholomeus Eustachius had used the description previously, his work however, was not published until the eighteenth century. In 1619, Hieronymus Fabricius ab Aquapendente recognized that goitres arose from the thyroid gland. Many functions were imaginatively ascribed to the thyroid gland, including lubrication of the larynx, providing a reservoir of blood to prevent engorgement of the brain, or beautifying women's necks.

Treatment of goitre was varied. Marine preparations, such as burnt seaweed, were among the most effective. In 1811 Bernard Courtois discovered iodine in the ash of burnt seaweed. Surgery of goitres was hazardous, with an exceedingly high complication and mortality rate. The first accounts of thyroid surgery were given by Roger Frugardi in 1170.

Failing response to medical treatments, two Setons were inserted at right angles into the goitre and tightened twice daily until the goitre separated. The open wound was then treated with cauterizing caustic powder and left to heal **(Dadan & Nowacka, 2008).**

From 1200 – 1700 AD, progress in thyroidectomy and surgery as a whole was impeded by church interference in university legislation. As a result, surgery became separated from medicine and began to be controlled by uneducated people such as barbers who evacuated abscesses and did blood-lettings and bone setters who set broken bones (Instytut Historii Nauki PAN., 1994). This is the origin of the reference of British surgeons as "Misters" instead of "Doctors". The first reliable description of successful thyroidectomy dates back to the tenth century when Albucasis, using opium sedation, removed a large goitre of a man who was seated with a bag around his neck to catch the blood **(Abulcasis, 1968)**. The first partial thyroidectomy was performed by Pierre Joseph Desault in 1791 **(Desault PJ. Giraud, 1792).** Other surgeons followed him, like Dupuytren in 1808, William Blizard in 1811 and Henry Earle in 1823. Heusser performed 35 thyroidectomies between 1842 and 1859 with 1 death. Victor von Bruns of Tubingen was the first to separate the isthmus from the gland and performed 28 thyroidectomies between 1851 and 1876 with 6 deaths.

Halsted's review of cases performed before 1850 found a mortality rate of 40%. This was caused by hemorrhage, airway obstruction in consequence of tracheal compression, overt postoperative infection and air embolism **(William S. Halsted, 1919.).** The later parts of the nineteenth century were associated with improved morbidity and mortality indices for thyroidectomy owing to the introduction of anesthesia, infection prophylaxis and improved hemostasis. Sulfuric ether was used as an anesthetic for the first time in 1842 by Crawford W. Long in Georgia. This was used three years later, 1845, in a successful thyroidectomy

performed by Nikolai Pirigoff in St. Petersburg (Chelius, 1847). In 1867, Joseph Lister of Glasgow used carbonic acid as an intraoperative antiseptic agent. This led to a significant decrease in infectious incidents in postoperative period. The introduction of caps and gowns by Gustav Neuber in 1883 and steam sterilization of instruments by Ernst von Bergmann in 1886 further improved on infection control efforts. A landmark in surgery in general was set in 1874 by Spencer Wells and Jules Pear by their invention of the first effective hemostatic forceps (Harvey, 1929). These innovations were gradually incorporated into the practices of the pioneer thyroid surgeons.

The most notable thyroid surgeons were Emil Theodor Kocher (1841–1917) and C.A. Theodor Billroth (1829–1894), who performed thousands of operations with increasingly successful results (Becker, 1977). As patients survived longer, however, problems emerged that had not been previously encountered. After total thyroidectomy, patients became myxedematous with cretinous features; the changes were more noticeable in children. Kocher coined the term “cachexia strumipriva” and wrongly attributed it to operative tracheal trauma giving rise to chronic asphyxia. Felix Semon suggested that myxedema was secondary to the loss of thyroid function, a view originally treated with skepticism. This was later proved true by Victor Horsley's studies on monkeys undergoing total thyroidectomy. The first successful treatment of myxedema was achieved in 1891 by George Murray when he prepared an extract of sheep's thyroid that he injected subcutaneously into a patient. Even at this early stage, differences in post-operative outcomes based entirely on surgeon factors were evident between Theodor Billroth and Theodor Kocher. Few of Billroth's patients developed myxedema, but William Halsted suggested that this was because of a difference in operative technique (Gley, 1988).

Kocher was extremely neat and precise, operating slowly in a bloodless field. He removed all the thyroid and his patients developed myxedema but rarely suffered laryngeal nerve damage or postoperative tetany. Billroth, however, worked rapidly and with less concern for hemorrhage. He often removed the parathyroid glands but left more thyroid tissue and therefore encountered postoperative hypoparathyroidism but rarely myxedema

Changes in thyroid surgery in the late 19th and early 20th centuries reflected the surgeons' appreciation of the various postoperative complications and their determinants. Halsted and Evans, who in 1907 published their observations on the parathyroid blood supply, advocated "ultra-ligation" of the thyroid arteries distal to the points of parathyroid artery takeoff as well as avoidance of inferior thyroid artery trunk ligation (William S. Halsted, 1919.). The technique of leaving a portion of the posterior thyroid capsule undissected near the ligament of Berry suggested by Jan Mikulicz Radecki, a student of Billroth, prevented recurrent laryngeal nerve damage. Diagnosis of damage to this nerve was made possible by the invention of indirect laryngoscope by the Spanish singer Manuel Garcia in 1854 (Haeger, 2000). Damage to external laryngeal nerve after thyroidectomy was recognized after the case of the opera singer Amelita Galli-Curci in 1936.

Surgery for toxic goitres was considered unsafe till 1884 when Ludwig Rehn of Frankfurt-am-Main reported 3 patients cured of their toxic symptoms incidentally when their goitres were removed for impending obstruction. Several strategies were subsequently developed in an effort to minimize the known danger of a thyroid crisis. Kocher used preliminary ligation of the thyroid arteries to provide for greater safety in the operation. Hartley was among the first to use partial surgical removal of the second lobe in a select number of patients while Mayo was an advocate of unilateral or bilateral pole ligation as a

preliminary to partial thyroidectomy in severe thyrotoxicosis. Dunhill suggested a second lobectomy in thyrotoxic patients after failure to respond to their initial procedure. Plummer published his results in using Lugol's iodine preoperatively in 600 thyrotoxic patients in 1923. He showed that the introduction of iodine caused a drop in operative mortality rate from approximately 4% to 1% (Plummer, 1923). Moreover, the introduction of radioactive iodine by Means, Evans and Hertz and its use therapeutically in 1942, thioruacil by Edwin Bennet Astwood in 1943 and the introduction of propranolol in 1965 contributed to considerable changes in perioperative procedures.

The diagnosis of thyroid disease was made more precise with the development of radiology especially of ultrasound and computerized tomography scanning. It became further improved with the introduction of fine needle aspiration cytology which was described by Soderstrom in 1952 (Nuland, 1988). Recent developments in thyroid surgery as of the year 2000 include: video-assisted thyroidectomy, total thyroidectomy of benign goitres, a transplantation of accidentally removed parathyroid glands in the ipsilateral sternocleidomastoid muscle, and intraoperative electro-identification of the recurrent laryngeal nerves and mini-invasive operations of thyroid gland. Despite the huge development of diagnostic and therapeutic techniques, some of the thyroid diseases need to be treated surgically.

2.2 Anatomy and Physiology of the thyroid Gland

Anatomy

The thyroid gland is a butterfly-shaped structure located in the central compartment of the neck. It is made up of right and left lobes on either side of the trachea, connected by the

isthmus. The isthmus is located just below the cricoid cartilage. It usually weighs an average of 14 – 25 grams. Enlargement of the thyroid, which is common in many thyroid disorders is referred to as goitre. Goitres can compress the trachea leading to compromised airflow. The thyroid gland receives a rich blood supply principally from the paired superior and inferior thyroid arteries and its anterior surface is covered by an extensive venous plexus. This explains the relatively high incidence of bleeding complicating the postoperative period. Added to this, there are strong fascial and muscular layers anterior to the gland which serve to create a confined space that can quickly build up pressure if bleeding occurred. This pressure transmits to the trachea and leads to airway obstruction. Posterolateral to the thyroid runs the recurrent laryngeal nerve (RLN) that controls the vocal cords. In this way, the nerve controls speech, phonation and airway opening and closing. The RLN has a close anatomical relation with various vascular, fascial-ligamentous and lymphatic structures around the thyroid (Standring & Gray, 2008). Injury to the nerve occurs inadvertently as these structures are manipulated. Other neural structures around the thyroid gland that can be injured during thyroidectomy include the superior laryngeal nerve and the cervical sympathetic chain. The posterior surface of the thyroid is also the location of the two paired parathyroid glands. These glands produce the parathyroid hormone that regulates body calcium levels. The parathyroid glands are situated either on the surface of the thyroid or within its substance or in its near vicinity. They additionally share a blood supply with the thyroid gland. Damage to the parathyroid glands occurs due to interference with their blood supply or direct trauma. The glands can also be resected inadvertently along with thyroid tissue. These insults lead to hypocalcaemia.

Physiology

The thyroid contains two thirds of the body's iodine – an essential component of the thyroid hormones, tetraiodothyronine (T4) and triiodothyronine (T3) (Hetzel BS, 1999). Within the thyroid follicle, the basic structural unit of the thyroid gland, iodine is oxidized and bound to tyrosine residues in thyroglobulin to form colloid. Colloid acts as the storage form of thyroid hormone. Daily, about 1% of the stored thyroid hormone is released into circulation. Thyroid stimulating hormone (TSH), a pituitary derived peptide, stimulates all the steps of thyroid hormone synthesis and secretion, including iodide transport, synthesis of thyroglobulin, iodination of thyroglobulin, and secretion of thyroid hormones. TSH and the thyroid hormones have an inverse log relationship. Small changes in T4 and T3 serum concentrations lead to large changes in TSH levels.

Thyroid hormones regulate many important biochemical reactions, including protein synthesis and enzymatic activity, and are critical determinants of metabolic activity (Council, 2005). They are also required for proper skeletal and central nervous system development in fetuses and infants (Trumbo, Yates, Schlicker, & Poos, 2001). Thyroid diseases can result in thyroxine over secretion or under secretion. When over secreted, the resulting clinical condition is called hyperthyroidism and its symptoms include: heat intolerance, weight loss, palpitations, hair loss and diarrhea. Under secretion results in a condition called hypothyroidism. It presents clinically with weight gain, fatigue, cold intolerance, constipation, hoarseness, growth and mental retardation in childhood.

Calcitonin appears to be involved in the maintenance of optimum blood levels of calcium but its precise role is unclear (Barrett, Barman, Boitano, & Brooks, 2009). Absence of

calcitonin doesn't seem to adversely affect calcium homeostasis. Measurement of calcitonin blood levels is important as it serves as a tumor marker for medullary carcinoma of the thyroid (Sadler & Dudley, 2000).

2.3 Preoperative evaluation of goitres

The fundamental goal of evaluation and management of patients with goitre is robust cancer screening and ensuring that surgery is only offered to those few patients who need it. A multi-disciplinary team consisting of surgeons, pathologists, endocrinologists and radiologists is required for optimal care (Ljung et al., 2008).

History and examination

The history should include an enquiry about the symptoms of hyperthyroidism, hypothyroidism, risk factors for cancer and symptoms due to glandular enlargement with compression to the aero-digestive tract.

The male gender and an age less than 30 years are believed to increase the risk of cancer in nodules >1cm (Frates et al., 2006; Silverman, Nussbaum, & Rausen, 1979). Other risk factors for cancer include: hypothyroidism; family history of MEN 2a and 2b; history of exposure to ionizing radiation to the head and neck during childhood. Additionally, the finding of hoarseness of voice in association with goitre raises the specter of cancer.

Compressive symptoms include: dyspnea, stridor, orthopnea, dysphagia and hoarseness of voice. Physical examination should elicit the goitre size, location of nodules and any associated lymphadenopathy. Ideally, all patients should have a preoperative laryngoscopic

examination. Preoperative recurrent laryngeal nerve paralysis can be a marker of invasive carcinoma (Gregory W Randolph, 2010).

Radiology

Evidence shows that examination for thyroid nodules by palpation has a poor sensitivity when compared to the use of ultrasound (Marqusee et al., 2000). The prevalence of asymptomatic thyroid nodules detected by ultrasound is 67% while physical examination identifies thyroid nodules in only 5-8% of cases (Tan & Gharib, 1997). Thus ultrasound is the most sensitive and specific technique to determine size, number, distribution and architecture of thyroid nodules. Ultrasonic features predictive of cancer include: nodule size >1cm; irregular margins; parenchymal hypo echogenicity and micro calcification (Moon et al., 2008). The American Thyroid Association currently recommends an ultrasound examination for all patients with goitre. Cross-sectional imaging i.e. CT scan and MRI is useful when there is a concern about invasive cancer and when substernal goitres have an upper airway obstructive component.

Serum TSH is the most sensitive method for detecting thyroid dysfunction assuming an intact hypothalamic-pituitary axis (McCullough, 2004). Patients found to have hyperthyroidism should undergo thyroid scintigraphy. This is most commonly done using either Iodine^{123} or Technetium Pertechnetate 99mTc radionuclides. Following scintigraphy, patients are stratified into three categories based on radionuclide uptake i.e.: Grave's disease – diffuse uptake; Solitary toxic nodule – single foci of uptake; Plummer's disease – multiple foci of uptake. All "cold thyroid nodules" i.e. with no radionuclide uptake, are further evaluated by FNA.

Fine Needle Aspiration Cytology (FNAC)

The result of FNAC determines to a large extent whether a patient can be followed clinically or referred for surgery. Consequently, ultrasound guidance during the FNA procedure has been recommended in an effort to reduce false negative rates (Danese, Sciacchitano, Farsetti, Andreoli, & Pontecorvi, 1998)

The indications of FNAC include: nodules >1–1.5 cm unless cystic; nodules <1cm but with ultrasound features suggestive of cancer; "cold" nodules on scintigraphy. In addition, FDG–PET and Sestamibi scan incidentalomas should be aspirated as they carry a cancer risk estimated at 14 – 66% (Alonso et al., 1996; Cohen et al., 2001). In patients with thyroid nodules >4cm diameter, FNA has been found to be highly inaccurate. The recommendation is that a diagnostic lobectomy, in the minimum, should be performed irrespective of FNAC result (McCoy et al., 2007). Multinodular goitres require that up to four nodules >1cm be aspirated for the accurate diagnosis of thyroid cancer. This should be ultrasound guided (Frates et al., 2006).

There is no role for core needle biopsy in the routine evaluation of low–risk thyroid nodules. Rarely, it is used when there have been multiple non–diagnostic FNAs and in tumor subtyping with an initial FNA suggesting thyroid lymphoma (Sanchez & Selvaggi, 2006). It is however associated with higher rates of hematoma, pain and damage to the trachea and recurrent laryngeal nerve.

FNAC should be reported according to six diagnostic terms defined by the 2010 Bethesda criteria (Ali & Cibas, 2010). Each of the categories has an implied cancer risk that links it to an evidence–based management guideline. This is highlighted in Table 1 below:

Table 1: The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

Diagnostic Category	Risk of Malignancy (%)	Usual Management
Nondiagnostic or unsatisfactory	1-4	Repeat FNA with ultrasound
Benign	0-3	Clinical follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	5-15	Repeat FNA
Follicular neoplasm or suspicious for a follicular neoplasm	15-30	lobectomy
Suspicious for malignancy	60-75	Near Total Thyroidectomy or lobectomy
Malignant	97-99	Near Total Thyroidectomy

A summary of the pathology of thyroid nodules sub classified to correlate with the Bethesda system is given in Table 2 below:

Table 2: Thyroid Pathology

I. Nondiagnostic or Unsatisfactory
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, etc.)
II. Benign
Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
Consistent with granulomatous (subacute) thyroiditis
Other
III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance
IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm
Specify if Hurthle cell (oncocytic) type
V. Suspicious for Malignancy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other
VI. Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma
Carcinoma with mixed features (specify)
Metastatic carcinoma
Non-Hodgkin lymphoma
Other

From Ali SZ, Cibas ES: *The Bethesda System for Thyroid Cytopathology: definitions, criteria, and explanatory notes,* New York, 2009, Springer.

FNA can decrease the need for surgical thyroidectomy by 30–50% while increasing the diagnostic yield of surgery i.e. ratio of total number of patients with carcinoma to the total number of cases operated (Gharib & Goellner, 1993). Currently, about half of patients recommended for surgery on the basis of an abnormal FNA cytology prove to have benign

disease. FNA has false negative and false positive rates of 5% and 1% respectively (Hall, Layfield, Philippe, & Rosenthal, 1989). FNA has a sensitivity of 43–98%; specificity of 72–100%; Positive predictive value of 89–98% and a negative predictive value of 94–99%. These values vary depending on the handling of indeterminate categories (Lewis, Chang, Pitman, Faquin, & Randolph, 2009).

Molecular markers such as BRAF, RET–PTC, RAS, galactin–3 and whole genome analysis have been used in an effort to increase the diagnostic yield. These markers are plagued by poor accuracy.

Summary

There is no single modality of evaluation that is likely to prove perfectly predictive of benign and malignant disease. A multivariate approach that combines clinical, sonographic, cytological and molecular assessments is likely to be most successful (OKAMOTO et al., 1994).

2.4 Indications of Thyroidectomy

The indications of thyroidectomy vary with the classification of goitres into simple, toxic, inflammatory or neoplastic. Common indications in all of these classes of goitres include signs and symptoms of compression, cosmetic disfigurement and general discomfort in the neck. All of these symptoms generally relate to the size of the goitre which in turn correlates with the 1986 World Health Organization (WHO) clinical grading of goitres (Delange et al., 1986; World Health Organization, 1994). Size dependent symptoms and signs of goitre worsen with higher grade. This grading is given below:

- **Grade 0 –** no goitre presence is found (the thyroid impalpable and invisible)
- **Grade 1a –** thyroid gland though palpable, remains invisible, even in full neck extension (the gland is not enlarged)
- **Grade 1b –** Palpable in normal position and visible in the upright position (full extension) of the neck; nodular goitres are also classified into this size range, even if they do not meet the criteria for enlargement.
- **Grade 2 –** visible in normal position of neck; no palpation required to diagnose the enlargement
- **Grade 3 –** Very large goitre, clearly visible from a distance.

Indications of thyroidectomy in non-toxic goitres

Diffuse non-toxic goitres are usually managed medically with iodine supplementation, eradication of the offending goitrogen and thyroxine to accelerate the process. Partial thyroidectomy is indicated on cosmetic grounds, pressure symptoms and discomfort. Multinodular non-toxic goitres are similarly managed. Extent of surgery in this case depends on number of nodes present. Management of solitary non-toxic nodular goitres should include an FNA to differentiate benign from neoplastic and solid from cystic. Total lobectomy is indicated for FNAC results showing follicular adenoma as this can't be reliably differentiated from follicular carcinoma on cytological grounds. Large solitary thyroid cysts carry a risk of sudden airway obstruction due to intracystic hemorrhage and are dealt with electively by lobectomy and/or isthmusectomy depending on their location. Total thyroidectomy is indicated for glands with widespread cystic involvement.

Indications of thyroidectomy in toxic goitres

Total thyroidectomy is currently the treatment of choice for patients with large toxic multinodular goitres. The thyroid function in these patients is very labile during treatment with antithyroid drugs and there is an over 50% relapse rate on withdrawal (Sadler & Dudley, 2000). In addition to this, radioiodine uptake is variable with minimal impact on goitre size and a general slow response. In toxic diffuse goitres (Graves' disease), the indications of thyroidectomy include large goitre size in patients under 45 years of age, failed medical treatment, goitre with thyrotoxic eye disease (exophthalmic goitre) and childhood Graves' disease (Williams, Bulstrode, & O'Connell, 2008). In western countries, there is a preference to the use of radioiodine in patients >45years fearing its perceived cumulative carcinogenic effects in those <45 years.

Thyroidectomy may also be indicated in thyrotoxicosis occurring in pregnancy when the disease is moderate to severe and especially when cardiac symptoms herald possible cardiac failure late in pregnancy. Failure of medical therapy is considered to have occurred in Graves' disease when there is a relapse of thyrotoxicosis after 12-18 months of treatment with antithyroid drugs or when there is poor compliance to the same drugs or unacceptable side effects. Exophthalmic goitre usually occurs in the setting of florid thyrotoxicosis which is difficult to control medically. In addition, the disease represents a relative contraindication to radioiodine treatment as this may lead to a deterioration of eye disease. Surgery is the treatment of choice for patients with toxic solitary nodular goitres who are under 45 years of age.

Indications of thyroidectomy in special (Inflammatory) goitre

Inflammatory goiters generally cause a transient hyperthyroidism before later leading to a hypothyroid state. Surgery is thus used with caution. Symptoms arising due to pressure on the trachea and esophagus are usually relieved by administration of varying combinations of prednisolone, aspirin, beta blockers and thyroxine. In Hashimoto's thyroiditis, total lobectomy or total thyroidectomy is indicated in patients with clinical or cytological suspicion of concomitant thyroid malignancy. In De Quervain's thyroiditis, surgery is only required if the diagnosis is equivocal on FNA. Surgery is required in Riedel's thyroiditis to exclude malignancy and to relieve severe constriction of the airway (Sadler & Dudley, 2000).

Indications of thyroidectomy in neoplastic goitre

Surgery is generally indicated whenever a diagnosis of carcinoma is suspected. The indication and extent of surgery will depend primarily on histological type, but age of onset and mode of presentation will influence management (Sadler & Dudley, 2000). Total lobectomy is indicated with low risk solitary macroscopic tumors and is considered the minimum conservative approach. Total thyroidectomy, on the other hand, is indicated for macroscopic multifocal disease with extrathyroidal invasion and demonstrable lymph node disease. In some diagnoses like malignant lymphoma and anaplastic carcinoma, the role of surgery may be limited to establishing a diagnosis.

2.5 Contraindications to thyroidectomy

These are few and mostly relate to the presence or risk of hypothyroidism. This is especially true where long term or lifetime thyroxine supplementation isn't feasible. As

such, most contraindications to thyroidectomy are relative rather than absolute. Traditionally, these included inflammatory goitres, autoimmune goitres with high antithyroid antibody titers and established hypothyroidism. The presence of high titers of thyroid antibodies indicates lymphatic infiltration of the goitre, i.e. a diffuse or focal thyroiditis, and a tendency to spontaneous remission. These patients are best treated with anti-thyroid drugs but, if medical treatment fails, definitive treatment by operation or radioiodine is not contraindicated (Williams et al., 2008). Steroids may help to reduce pain and swelling.

Extensive local and distant spread of thyroid malignancy represents a further contraindication to thyroidectomy. This includes dermal metastases to skin of neck, intracranial tumor spread, fixation of tumor to skull base, internal carotid arteries and the cervical spine.

2.6 Standard thyroidectomy procedure (Conventional Thyroidectomy)

The surgical approach to the thyroid gland is by a collar incision usually placed 2.5cm above the suprasternal notch. Superior and inferior sub-platysmal flaps are then raised extending dissection to the thyroid cartilage and the sternal notch respectively. The midline raphe between the strap muscles is then identified and the muscles parted. In the case of large goitres, the strap muscles could be divided.

The middle thyroid veins are ligated and divided first whenever found. The superior thyroid pedicle is then individually ligated and divided after retracting it downward and laterally to identify the external branch of superior laryngeal nerve. With careful technique, the nerve can be found in 90% of cases (Aina & Hisham, 2001). This identification is

important as studies have noted that objective evidence of superior laryngeal nerve injury is hard to demonstrate by routine laryngoscopic examination (Delbridge, 2003). Patients with injury to this nerve suffer reduced voice range, lower pitch and vocal fatigue.

There has been a shift from "lateral dissection" to "capsular dissection". The former, which was common in the 1970s, led to higher rates of recurrent laryngeal nerve injury during its extensive exposure (Bliss, Gauger, & Delbridge, 2000). The parathyroid glands were also commonly devascularized leading to hypocalcemia. Capsular dissection involves beginning the lateral component of dissection high on the thyroid gland's surface and development of a plane between the thyroid capsule and the inferior thyroid artery. In this way, the recurrent laryngeal nerve is "encountered" rather than dissected for. This dissection type also enables recognition of sympathetic-laryngeal nerve anastomoses. Intracapsular or subcapsular dissection is a variant technique in which the dissection plane is medial to the thyroid capsule. It finds common usage in sub-total thyroidectomies. There is a tendency to avoid nerve visualization with this method i.e. "a nerve if seen is injured" (Prioleau, 1933).

The inferior thyroid artery's penultimate branches are ligated and divided on the glandular surface thus preserving the blood supply to the parathyroid glands. Routine parathyroid auto transplantation is now an accepted standard of care (Delbridge, 2003) . The procedure is then completed according to the extent of surgery. In total thyroidectomy, there has been a change from an anatomically based approach to an embryological one. The latter involves ensuring completeness of resection by paying attention to: thyroglossal tract and pyramidal remnants; thyrothymic thyroid rests; tubercle of Zuckerkandl.

2.7 Minimally invasive thyroidectomy (MAT, MIVAT)

Generally, thyroidectomy technique mandates meticulous surgical dissection, absolute hemostasis, en bloc tumor resection and adequate visualization of the operative field. All of these principles can now be accomplished with minimally invasive techniques. Common to all minimally invasive methods is incisions less than 3cm long and use of alternative energy sources for hemostasis such as the ultrasonic scalpel, bipolar coagulation, or the electro thermal vessel sealing system. Surgery may be considered minimally invasive in respect of not only the length of skin incision but also the accessibility of the operative field and extent of dissection. Minimally invasive techniques have the advantages of less tissue trauma, shorter hospital stay, potential health care cost savings, reduced postoperative pain, patient comfort, and more attractive cosmetic results (Thomusch, Hoffmann, & Dobschuetz, 2006).

The techniques of minimally invasive thyroidectomy can be described as pure endoscopic or open. In the former, the thyroid is approached from a small incision in the axilla, mammary areola or anterior chest therefore avoiding unsightly incisions on the neck (Gagner & Inabnet, 2001). This can be with or without gas insufflation. Open techniques can either be with or without video assistance. The one without video assistance is given the acronym MATS i.e. Minimal Access Thyroid Surgery. In this, a central neck mini-incision is used to approach the thyroid gland. The advantage is that it can be done under local anesthesia (Allendorf et al., 2007). However, it has the disadvantage that the surgical site view is restricted to one person. Open techniques with video assistance take the acronym MIVAT i.e. Minimally Invasive Video Assisted Thyroidectomy. Though

performed under general anesthesia, MIVAT provides an excellent endoscopic view of the surgical field through a small incision.

Indications and contraindications of MAT and MIVAT

Indications are based on overall thyroid size, size and histology of thyroid nodules and thyroid volume. In cancer cases, additional factors include the presence of enlarged lymph nodes and evidence of loco-regional invasion. Inherent in their nature, minimally invasive techniques put a size limit to the goitres. These limits include: 30 cc in volume, thyroid nodule size of <4 cm in diameter and actual cancer size of <2 cm (Ruggieri et al., 2007).

As such, certain diagnoses constitute clear contraindications to minimally invasive techniques and on the converse necessitate standard thyroidectomy methods. These include: large cancers with loco-regional spread, history of inflammatory goitre where dissection may be compromised by tissue adherence and bleeding that precludes adequate visualization of the recurrent laryngeal nerve (RLN) and parathyroid glands, recurrent goitre and head/ neck irradiation. In addition, medullary thyroid cancer (MTC) patients should undergo conventional thyroidectomy with appropriate ipsilateral or bilateral functional neck dissection as these tumors are not radio-iodine sensitive and complete surgical resection is the centerpiece of management.

Surgeons who employ minimally invasive thyroid techniques must have considerable experience with open, conventional thyroid surgery, especially since outcome of thyroid surgery is directly linked to the experience of the operating surgeon (Henry, 2006; Sosa et al., 1998)

The demonstration of meaningful advantages for minimally invasive techniques over conventional surgery is not easy (Miccoli et al., 2001; Palazzo, Sywak, Sidhu, & Delbridge, 2005; Udelsman & Donovan, 2004). The overall complication rates are similar and only the mini open approach is more favorable than conventional operation in terms of surgical time(Udelsman & Donovan, 2004).

2.8 Postoperative complications and their determinants

The outcome and complication rates of thyroidectomy are largely dependent on surgeon's skill and experience, the extent of surgery, indication of surgery and number of thyroid surgeries performed at that particular center (McHenry, 2002). The complications relating to damaged individual structures can be kept to a minimum by operating in a bloodless field and performing a meticulous anatomical dissection (S. I. Schwartz, Kaplan, & Schwartz, 1999).

Recent studies give mortality rate of 0.5% and morbidity rates less than 3% (Lombardi et al., 2007). David A.K. et al in a review article entitled "thyroid surgery in the tropics" noted that thyroid surgery in the tropics was carried out by either general surgeons or ear, nose and throat surgeons. Few places had subspecialist endocrine or head and neck surgeons. Additionally, diagnostic aids like cytology service and radiology were not readily available. The choice of operation, in addition to being determined by the local thyroid pathology, was also influenced by the likelihood of being able to obtain lifelong thyroxine. As such, total thyroidectomy was avoided whenever thyroxine supplies were unreliable. Despite these drawbacks, it was noted that with proper training, thyroid surgery

could be carried out safely with minimum complications even in remote mission hospitals with limited facilities for investigation. Post-operative complication rates comparable to those in the developed world could be achieved i.e. mortality - 0%, permanent recurrent laryngeal nerve (RLN) injury less than 2%, re-exploration for hematoma less than 2%, permanent hypocalcaemia less than 5% and wound infection - 2.5% (Watters & Wall, 2007). Thyroidectomies performed at Mission hospitals were noted to be associated with lower rates of morbidity and mortality that approached international figures in the study by David A.K. et al. In a 2004 local retrospective study by L. Wagana et al, mortality rate of 0.5% and morbidity rates of 3.6% were found (Hill et al., 2004). It involved 220 thyroidectomies that had been performed at Kijabe Mission Hospital between 1st Jan 1999 and 31st Dec 2001. They reported a RLN injury rate of 1.4% and they emphasized capsular dissection and identification of the recurrent laryngeal nerve as prerequisite to avoiding injury. This view is supported by other studies (Hayward, Grodski, Yeung, Johnson, & Serpell, 2013; Idris et al., 2013).

The three main complications of thyroidectomy reported are hypocalcaemia, Recurrent Laryngeal Nerve injury and postoperative bleeding. Other less frequent early post-operative complications are airway obstruction, surgical site infection, hypothyroidism, seroma formation, flap edema, thyroid storm, stitch sinus and granuloma.

2.8.1 Hypocalcaemia

Post-operative hypocalcaemia is mostly due to inadvertent removal, accidental injury or devascularisation of the parathyroid glands during thyroidectomy. Traditionally, this was prevented by maintaining the parathyroid glands in situ on a vascularized pedicle. The branches of the inferior thyroid artery were individually ligated on the surface of the

thyroid and the glands left undisturbed in their envelope of fat (McHenry, 2002). It is now recognized that, not only is dissection of parathyroid glands on a vascularized pedicle a very time consuming process, especially for those situated high on the thyroid surface, but it does not necessarily guarantee their preservation. Many a parathyroid gland that has been painstakingly dissected on a long pedicle simply infarcts later on as a result of thrombosis of the tenuous vascular supply, or as a result of edema and swelling of the gland within its dissected capsule (Delbridge, 2003).

Another cause of post-operative hypocalcaemia is 'hungry bone disease'. This occurs in the setting of hyperthyroidism that was preoperatively managed with beta blockade rather than normalization of serum thyroxin. It results in rapid influx of serum calcium into bones (Williams et al., 2008). In overt hyperthyroidism, osteoclastic bone resorption is stimulated out of proportion to osteoblastic reminerization (Eriksen, 1986). These effects are as a result of direct actions of T3 and TSH on bone. There may also be a contribution from raised IL-6 levels, observed in hyperthyroidism, that stimulates osteoclast production. The result is loss of bone mass (Lakatos et al., 1997). The sudden postoperative withdrawal of thyroid hormone induces a stop in osteoclastic bone resorption without affecting the osteoblastic activity. Consequently, an increased bone uptake of calcium, phosphate and magnesium is observed i.e. hungry bone syndrome. Other suggested contributory factors to post-operative hypocalcemia include hemodilution secondary to intravenous fluid administration during perioperative phase, increased urinary calcium excretion secondary to surgical stress and calcitonin release after thyroid gland manipulation (Jessie & Harrison, 2010).

Hypocalcemia occurs at rates between 0.33 – 65% (Bhattacharyya & Fried, 2002; Bron & O'Brien, 2004; Mehanna, Jain, Randeva, Watkinson, & Shaha, 2010; Ozbas et al., 2005; Qureshi et al., 2001; L. Rosato et al., 2002). This wide range is explained by variant definitions for post-thyroidectomy hypocalcemia in literature. Patient case mix is an additional consideration. Examples of this is the observed higher rates of hypocalcemia in thyrotoxic patients due to hungry bone disease and the occurrence of latent vitamin D deficiency in patients residing in latitudes above 50º (Mehanna et al., 2010). Lack of a standardized definition of hypocalcemia prevents meaningful comparisons of results and pooling of data when performing meta-analyses. A proposed definition and one which has been adopted for use in this study is given: Postop hypocalcemia is an adjusted serum calcium level at any point after the operation below the institution's reference range, requiring treatment with vitamin D derivatives and/or calcium supplements, to correct falling calcium within institutional reference range and/or treat symptoms. This definition is informed by the observation that only one third of patients with biochemical hypocalcemia require treatment due to symptoms which generally arise at serum calcium levels below 7.5mg/dl (Bron & O'Brien, 2004; Mehanna et al., 2010; A. R. Zambudio et al., 2004).

Hypocalcaemia can be temporary or permanent with a suggested cut-off of 6 months or more(Mehanna et al., 2010). Rates of this complication were notably higher after total thyroidectomy. Hypocalcaemia following thyroidectomy is usually temporary. Delbridge et al. stated that transient hypoparathyroidism should be an accepted outcome of bilateral thyroid surgery rather than a complication(Delbridge, Guinea, & Reeve, 1999). It is noted that the degree and duration of hypoparathyroidism increase with the extent of thyroid

surgery. Ozbas and colleagues reported that the incidence of temporary hypoparathyroidism had increased with the extent of the surgery. However, they also reported that extent of the surgery had no effect on permanent hypoparathyroidism. This was better correlated with the management of the parathyroid glands (Ozbas et al., 2005). The incidence of permanent hypoparathyroidism should be less than 1% and most cases present dramatically 2-5 days after operation. However, very rarely the onset is delayed for 2-3 weeks or a patient with marked hypocalcaemia is asymptomatic. Peri-oral tingling is generally the first and most sensitive indicator of a low serum calcium. Paraesthesia in the fingers and toes preceding frank tetany is seen when hypocalcaemia is profound. The serum calcium concentration should be monitored postoperatively as patients without overt hypoparathyroidism may develop vague lethargy and depression, insidious cataracts, mental deterioration, and psychosis. Hypocalcaemia should be evident by one week post-operative and is suspected in patients who are unduly agitated or depressed or hyperventilate. A positive Chvostek–Weiss sign and Trousseau's sign are valuable clinical adjuncts. Severe hypocalcaemia warrants intravenous infusion of 10 ml of 10 per cent calcium gluconate (given slowly to avoid cardiac arrest in systole). This infusion may need to be repeated every 4–6 hrs. Oral effervescent calcium, 4 to 6 g daily, should also be administered, depending on response. If hypocalcaemia persists, vitamin D (calciferol 25 000–100 000 units) and 2 to 3 g oral calcium per day are given until a normocalcaemic state is achieved (Sadler & Dudley, 2000).

Wells et al in 1975 demonstrated both clinically and biochemically the effectiveness of parathyroid auto-transplantation (Wells, Gunnells, Shelburne, Schneider, & Sherwood, 1975). Since then, it became routine to selectively auto-transplant parathyroid glands into

the ipsilateral sternocleidomastoid muscle. Parathyroid glands were chosen for auto-transplantation based on the anticipated difficulty in their dissection or on their dubious viability after dissection. However, even more recently, there has been an observation that the viability of in situ vascularized parathyroid glands remains unpredictable with late ischemia always a possibility. Consequently, there is now a trend for the routine auto-transplantation of at least one parathyroid gland during every total thyroidectomy (Zedenius, Wadstrom, & Delbridge, 1999). While unnecessary in most cases, it provides insurance in cases where late ischemia of the remaining glands actually occurs. Routine auto-transplantation is associated with an increase in the rate of temporary hypocalcaemia in the short term but has, in theory, the potential to reduce permanent hypoparathyroidism to zero (Lo, 2002).

2.8.2 Recurrent laryngeal nerve injury

Recurrent laryngeal nerve (RLN) injury follows accidental transection, crushing, tying, cauterization by diathermy or even just stretching or kinking of the nerve intraoperatively. The anatomical site most associated with these injuries is the ligament of Berry (Delbridge, 2003). Previously, routine exposure of the recurrent laryngeal nerve throughout its course had been shown to reduce the nerve's injury rates (Hermann, Alk, Roka, Glaser, & Freissmuth, 2002). However, later observations showed that the blood supply to both the parathyroid glands and the nerve itself were compromised in doing so. In addition, the nerve was additionally injured by neuropraxia due to prolonged handling (Delbridge, 2003). Refinement of surgical technique with capsular dissection evolved to combat these challenges. This involves commencing the lateral component of the dissection high on the

surface of the thyroid gland, dividing only the tertiary branches of the inferior thyroid artery and progressing posteriorly. An additional factor that may lead to injury of the RLN is the presence of a non-recurrent laryngeal nerve. This is more common on the right and takes a course similar to that taken by the inferior thyroid artery. It can thus be confused for the artery and ligated.

Internationally, rates of postoperative RLN paralysis ranges between 0 – 14% mainly due to differences in surgical expertise and nature of operation **(McHenry, 2002)**. Paralysis may be temporary or permanent, unilateral or bilateral. Temporary RLN paralysis rate is reported to be between 2.6% and 5%. Identification of the RLN at surgery is reported as the fundamental step in avoiding injury **(Aytac & Karamercan, 2005).** Incidences of this complication rise with operation for thyroid malignancy, increasing goitre size, increasing extent of resection and reoperative surgery for recurrent goitres where it ranges between 3 – 18% (37). Aysun Simsek Celik et al reported that recurrent laryngeal nerve injury rates were higher in surgeries lasting more than 90 min (Simsek Celik et al., 2011). Clinically, loss of vocal power and huskiness is often evident for 2 or 3 days after surgery and is presumed to be due to edema. It is relieved by local anesthetic lozenges and/or humidified air. Persistence of symptoms may indicate neuropraxia, caused by stretching or crushing of the nerve. This is reversible and recovers over several weeks or months. Permanent damage will result if the nerve is divided or ligated and is more likely to occur when the anatomy is distorted, for example with recurrent or malignant goitres. Unilateral injury may be asymptomatic and pass undetected due to compensatory hyper adduction of the unaffected cord unless routine postoperative laryngoscopy is performed. Management strategy in this case may involve stabilization of the affected cord in adduction by the sub

mucous injection of Teflon under direct laryngoscopy. The effects of bilateral nerve injury are likely to be temporary but pose an immediate problem when the patient is extubated at the end of surgery since the unopposed adductor action of the cricothyroid muscles closes the glottis to such an extent that the least exertion results in obstruction. The patient must be promptly re-intubated, paralyzed, and ventilated whilst hydrocortisone is given, 100 mg three times daily, to combat the edema and inflammatory response. Failure of extubation in 48hrs warrants a surgical airway. Exploration and restoration of the nerve, with grafting when necessary, is now feasible, as is the anastomosis of the hypoglossal and recurrent nerves (Sadler & Dudley, 2000).

2.8.3 Postoperative bleeding

Postoperative bleeding is an important complication after thyroidectomy and may be the limiting factor for outpatient thyroid surgery or early discharge from hospital (Dralle, Sekulla, Lorenz, Grond, & Irmscher, 2004). The source of bleeding can be arterial, venous or diffuse. The location of the source of bleeding can be the thyroid remnant or thyroid bed, cervical muscles, sub fascial veins or subcutaneous tissue. In up to 6.8% of cases, no site of bleeding is found upon re-exploration (Promberger et al., 2012). Intraoperative bleeding is associated with the occurrence of postoperative bleeds and hematomas. It stains the tissues and obscures important structures and generally increases the risk of other anatomic complications.

The rate of postoperative bleeding as reported in literature stands at 0 – 5% **(Ozbas et al., 2005).** In a prospective study of 30,142 operations by R. Promberger et al titled " Risk factors for postoperative bleeding after thyroid surgery", the factors associated with bleeding were found to be: older age, male sex, extent of resection, bilateral procedure,

retrosternal goitre and operation for recurrent disease (Promberger et al., 2012). This study also showed that differences in the surgeon performing the procedure can account for over seven-fold difference in the rate of post-operative bleeding. Other studies agree with this (Sosa et al., 1998). The other finding was that the time interval between skin closure and diagnosis of bleeding ranged from 6hrs to 48 hours with a mean of 16 hours. They recommended that the patient be observed for a minimal of 24hrs post-operative. The morbidity and mortality was noted to increase when there was a delay in diagnosis. The bleeding related mortality rate was 0.01% overall. When patients had to be re-operated due to bleeding, the mortality rate rose to 0.6%. The initial signs and symptoms indicative of postoperative bleeding included blood in suction drain, swelling and hematoma in the neck, bleeding from incision, dyspnea, cyanosis and dysphagia. Drains which were used in all patients in this study on the premise that they would signal bleeding and decompress the neck were found to be the direct source of bleeding during their removal. Thus drains are no longer used routinely **(Sanabria et al., 2007).**

When bleeding and hematoma occur deep to the strap muscles and deep to the deep cervical fascia, the situation can rapidly develop into a life threatening emergency because of associated airway obstruction. This obstruction may be due to direct compressive effects on the trachea or due to development of supraglottic edema. Management of these deep hematomas involves urgent decompression by opening all the layers of the wound to relieve tension before urgent transfer to theatre to secure the bleeding structure. Supraglottic edema may necessitate fashioning of an emergency tracheostomy to secure the airway (Abbas, Dubner, & Heller, 2001). A subcutaneous hematoma or collection of

serum may form under the skin flaps and require evacuation in the following 48 hours. This minimizes risk of infection.

2.8.4 Airway Obstruction

Airway obstruction can occur early in the postoperative period. Reasons for this are varying and include: laryngospasms; laryngeal oedema due to manipulation; tracheal compression secondary to tension hematoma; laryngeal obstruction due to bilateral cord paralysis. Very rarely, it occurs due to collapse or kinking of the trachea which is mostly secondary to Tracheomalacia (Williams et al., 2008). This softening of the tracheal cartilages occurs after a long standing goitre especially if retrosternal. Such patients usually also suffer laryngeal edema and reduced movement of the vocal cords, following difficult intubation and delivery of the lobes. Whenever the trachea is markedly soft and narrow, an elective tracheostomy should be performed (Sadler & Dudley, 2000).

Most cases of post-operative airway obstruction are caused by laryngeal edema. This most importantly follows tension hematoma. However, trauma to the larynx by endotracheal intubation and surgical manipulation are important contributory factors, particularly if the goitre is very vascular, and may cause laryngeal edema without a tension hematoma. Injury to the recurrent laryngeal nerve, whether unilateral or bilateral, usually doesn't result in immediate post-operative airway obstruction unless laryngeal edema occurs concurrently (Williams et al., 2008). The injury nonetheless aggravates an already present airway obstruction.

Management of airway obstruction will depend on the cause. If releasing the tension hematoma does not immediately relieve airway obstruction, the trachea should be

intubated at once. The endotracheal tube is left in place for a few days as steroids are given to reduce laryngeal edema. Tracheostomy is indicated rarely in the case of a failed intubation. Repeated attempts at intubation in the setting of laryngeal edema are discouraged as they may aggravate the problem. In a crisis situation, performing a needle tracheostomy using a 12G intravenous cannula as a temporary measure is considered satisfactory.

2.8.5 Post-operative Hypothyroidism

Hypothyroidism in general is caused by the following conditions: autoimmune thyroiditis; iatrogenic under which is thyroidectomy, radioiodine therapy and drug induced e.g. lithium and thionamides; dyshormonogenesis; goitrogens; secondary to pituitary or hypothalamic disease; thyroid agenesis and resistance to thyroid hormone (Williams et al., 2008). The most common cause of hypothyroidism after thyroid operation is subtotal resection for Graves' disease or multinodular goitre with autoimmune destruction of the remnant thyroid tissue being the underlying mechanism (Lal & Clark, 2005). Hypothyroidism is rare after surgery for a toxic adenoma because there is no autoimmune disease present. It is however inevitable after total thyroidectomy. Remnant tissue size seems to be important in prediction of outcome of operation, but within optimal remnant size the only factors which have an effect on the risk of hypothyroidism are lymphocytic infiltration of the thyroid tissue and antithyroid microsomal antibody titer (Huang, Wang, Shun, & Liaw, 1995). With optimal remnant size the higher the antithyroid microsomal antibody titer and the degree of lymphocytic infiltration, the greater the likelihood of post-operative hypothyroidism.

The incidence of postoperative hypothyroidism is considerably higher than was previously thought and rates of 20-45% at 10 years have been reported (Lando et al., 1990). Factors

such as increased age, operation type, histopathologic type, underlying disease, lymphocytic infiltration and use of levothyroxine before surgery are associated with the increased incidence of hypothyroidism (Lankarani et al., 2008). Avoiding hypothyroidism is one of the main challenges when operating for thyrotoxicosis. The factors outlined above affect how much thyroid tissue is left behind and this in turn determines risk of hypothyroidism or recurrent hyperthyroidism. In this setting, expected hypothyroidism rates are 10–15 per cent and below 5 per cent for persistent hyperthyroidism (Sadler & Dudley, 2000).

Hypothyroidism as a sequel of thyroidectomy remains unnoticed most of the time. It usually occurs within 2 years. Mild hypothyroidism after subtotal thyroidectomy may subside after a few months as the remnant thyroid tissue is stimulated by the rising TSH. Nearly all patients undergoing surgery for thyrotoxicosis become biochemically hypothyroid for 2 to 3 months after surgery. No correction is necessary as the majority will then stabilize in a euthyroid state. Clinical assessment should be maintained for at least 2 years, during which serum thyroxine and TSH concentrations should be monitored. Thyroxine supplementation is then given to those patients who become clinically hypothyroid. Routine administration of thyroxine (0.1 mg daily) is recommended for all patients undergoing surgery for non-toxic, diffuse, or multinodular goitres since failure to suppress TSH drive can result in recurrent goitre, even if hypothyroidism is subclinical.

2.8.6 Seroma formation

Seroma may be defined as a clinically identifiable collection of serous fluid within a surgical cavity in the postoperative period. In thyroid surgery, it presents as a central neck swelling and is confirmed by aspiration of serous fluid. Seroma formation after thyroid

surgery may lead to unsightly swelling, a suboptimal cosmetic result, and increased risk of infection. It occurs at an incidence of between 1.3 and 7%. Patrick Sheahan et al in an observational case–control study entitled: comparison of incidence of post-operative seroma between flapless and conventional techniques for thyroidectomy: a case-control study found that the flapless technique reduced the incidence of post-operative seroma. Seroma formation in this case was attributable to the extensive raising of skin flaps in the conventional thyroidectomy (Sheahan, O'Connor, & Murphy, 2012). Aysun Simsek Celik et al in a retrospective study of 332 patients who underwent thyroidectomy at a training and research hospital found that daily drainage more than 50 cc of blood increased the risk of seroma formation (Simsek Celik et al., 2011).

2.8.7 Surgical site infection

The rate of wound infection after thyroidectomy is underestimated but it is a likely complication in 2 - 7% of all cervical wall closures **(G. Dionigi, Rovera, Boni, Castano, & Dionigi, 2006).** Infections are classified as superficial (skin and subcutaneous tissue), or deep incisional (deep soft tissue: muscle and fascia), or those involving organs or body spaces (Horan, Gaynes, Martone, Jarvis, & Emori, 1992). Patients with surgical site infection should have early exploration and evacuation performed, and appropriate antibiotic cover instituted. Gianlorenzo Dionigi et al in a randomized prospective surveillance analysis study entitled Wound morbidity in mini-invasive thyroidectomy found that 100% of SSIs occurred after discharge from the hospital. He thus advised a post discharge patient surveillance that included recording any post discharge fever, wound discharge, wound pain, prescription of antibiotics, and visits to the emergency room,

general practitioner, or other physician for wound related concerns (G. Dionigi, Boni, Rovera, Rausei, & Dionigi, 2011). This study also showed a lower incidence of SSI in MIT as compared to Conventional thyroidectomy. It was hypothesized that the MIVAT procedure produced reduced surgical trauma to the cervical area due to the reduced length of the surgical incision, less stretch of the skin margins, a limited number of sutures, reduced tissue manipulation with a less pronounced pro-inflammatory response, and preserved immune system function, resulting in a reduced incidence of SSI (Wichmann et al., 2005). Overall, the risk of infection depended mainly on the quality of pre-operative and post-operative care and on whether there was a break in sterile technique. The use of drains and pre-operative antibiotics did not affect the incidence of SSI.

2.8.8 Flap edema

This complication is considered present with the finding of skin flap puffiness and swelling located about 1-2cm from the incision site (Wax, Valiulis, & Hurst, 1995). It is commonly noted on the superior flap and resolves after 2-3 months. Flap edema causes cosmetic disfigurement. This may be a source of concern when it is considered that there is an increasing societal focus on appearance and cosmesis (Chavatzas, 1975). Studies show that by using minimally invasive techniques, sub-platysmal flaps can be easily avoided in virtually all thyroid surgeries (Terris, Seybt, Elchoufi, & Chin, 2007). This has the potential to reduce the incidence of flap edema and prolonged wound healing.

A retrospective study by Aysun Simsek Celik et al found that flap edema rates were higher in patients who had a big gland size and operated by the resident surgeon as opposed to the specialist surgeon. This was related to inadequate surgical technique with damage of the

lymphatics in addition to poor venous circulation due to hemostatic over ligation (Simsek Celik et al., 2011).

2.8.9 Thyroid Crisis

This is an acute exacerbation of hyperthyroidism. Previously, thyroid crisis was a common complication of toxic goitre surgery during intraoperative and postoperative periods. Preoperative medical control of the thyrotoxic state and use of radioiodine ablation has greatly reduced this phenomenon. Today, thyroid crisis more commonly is seen in a thyrotoxic patient with intercurrent illness or non-thyroid surgical emergency (Williams et al., 2008). In the general hospitalized patients with thyrotoxicosis, the incidence of thyroid crisis is less than 10 percent (Nafisa K Kuwajerwala, 2010). Clinically, thyroid crisis is characterized by high fever, tachycardia (atrial fibrillation), extreme restlessness, and delirium. Management involves symptomatic and specific treatments. Symptomatic treatment is given for dehydration, hyperpyrexia, restlessness and cardiac symptoms. This involves intravenous fluid administration, external cooling of the body with ice packs, the administration of oxygen, diuretics for cardiac failure, digoxin for uncontrolled atrial fibrillation, sedation and intravenous hydrocortisone. Specific treatment is by administration of carbimazole, Lugol's iodine orally or sodium iodide intravenously. In addition, propranolol is given to block the peripheral adrenergic effects of thyroxine.

Early recognition and prompt intervention are necessary to prevail in management of this phenomenon. When fulminant and untreated, thyroid crisis is fatal. Even with improved

methods of diagnosis and treatment, mortality rates of 20–30% are reported (Carroll & Matfin, 2010).

3 Methodology

3.1 Introduction

This chapter describes the study setting, study design and study population. It outlines the methods used for data collection and analysis. It also outlines the inclusion and exclusion criteria and the ethical considerations.

3.2 Study setting

This study was carried out at Moi Teaching and Referral Hospital (MTRH) which is situated in Eldoret town, western Kenya. Its geographical coordinates are 0° 30' 44" North, 35° 16' 50" East. MTRH is the teaching hospital for Moi University and has a capacity of 800 beds. It serves not only the residents of Uasin-Gishu County but also those of the entire western region of Kenya. The population of this region, which includes North Rift valley, Nyanza and Western provinces, is estimated to be 15 million. MTRH also receives patients from Eastern Uganda and Southern Sudan.

Uasin Gishu district and the surrounding regions are highland areas of the Great Rift Valley. The altitude of these areas ranges from 1700 to 2400 metres. Eldoret town lies at an altitude of 2117 meters above sea level. The soil in these highland areas is deplete of iodine due to prior glaciation. Consequently, these areas have a high prevalence of endemic goitre. Currently all retailing table salt is iodized in an effort to reduce the rates of goitre. Some of the staple foods taken by communities in these regions contain goitrogens. These include sweet potatoes, kales, cabbages, soya beans, cassava and peanuts. These too could have contributed to the high prevalence of goitre previously seen here.

3.3 Study population

This included patients with goitre who presented for evaluation at MTRH general surgical and ENT clinics for a 1-year period (August 2012 - July 2013).

Inclusion Criteria

All patients with goitre who had indications for thyroidectomy

Exclusion criteria

- Patient mortality arising from anaesthetic complications of surgery.
- Thyroidectomy performed with emergency indications e.g. airway compromise, trauma to the thyroid
- Patients who are unable to give informed consent for surgery and/or the study, including minors and individuals who did not give assent and whose legal guardians did not give informed consent.
- Patients with prior irradiation to the neck.
- Patents with other non-thyroid head and neck tumours involving the anterior lower neck.
- Patients who undergo neck dissection

Sample size calculation

For descriptive studies in populations, Cochran developed the formula to yield a representative sample for proportions: which is valid where:

- n is the sample size,
- Z^2 is the abscissa of the normal curve that cuts off an area at the tails (1 – equals the desired confidence level, e.g., 95%),
- *e* is the desired level of precision – absolute precision of 5% will be considered to estimate the margins of error at which the results shall be acceptable.
- *p* is the estimated proportion of an attribute that is present in the population. (21% from a Greek study with comparable methodology)(A. R. Zambudio et al., 2004)

A response rate of 80% shall be considered adequate.

$$n = Z^2 \frac{p(1-P)}{e^2}$$

$$n = 1.96^2 \times \frac{0.21(1-0.21)}{(0.05^2)}$$

$$n = 255$$

Finite population correction for proportions

If the population is small (< 10,000) then the sample size can be reduced. This is because the given sample size provides proportionately more information for a small population than for a large population

Since the population was less than 10,000 the following formula was used to determine the desired sample size.

$$nf = \frac{n}{1 + \frac{n}{N}}$$

Where:

nf = the desired sample size (N<10,000) i.e. population less than 10,000

n = the desired sample size calculated previously (255)

N = total population (target) <10,000

As per the MTRH general surgery theatre records, an average of 74 thyroidectomies per year were done between 2010 and 2011 i.e. N = 74

Therefore:
$$nf = \frac{255}{1 + \frac{255}{74}}$$

$$nf = 57$$

Desired sample size was 57. In the end, all the 74 patients who consented were recruited into the study.

3.4 Sampling procedure

This was by a purposeful consecutive non probabilistic technique. It entailed recruiting all eligible patients presenting to the surgical outpatient department. No randomisation was be done.

3.5 Study design

This was an observational, cross sectional study.

3.6 Study Methods

Eighty patients with goitre presented to the MTRH general surgery and ENT clinics for evaluation between August 2012 and July 2013. Three patients declined to give consent for surgery and were excluded from the study. Similarly, two patients with a diagnosis of advanced anaplastic thyroid cancer were excluded as this constituted a contraindication of thyroidectomy. One additional patient was excluded due to the fact that he needed to have a modified neck dissection for lateral aberrant neck masses. All the remaining 74 patients were recruited into the study and proceeded to have preoperative, intraoperative and postoperative evaluations. The enrolment schema is presented below:

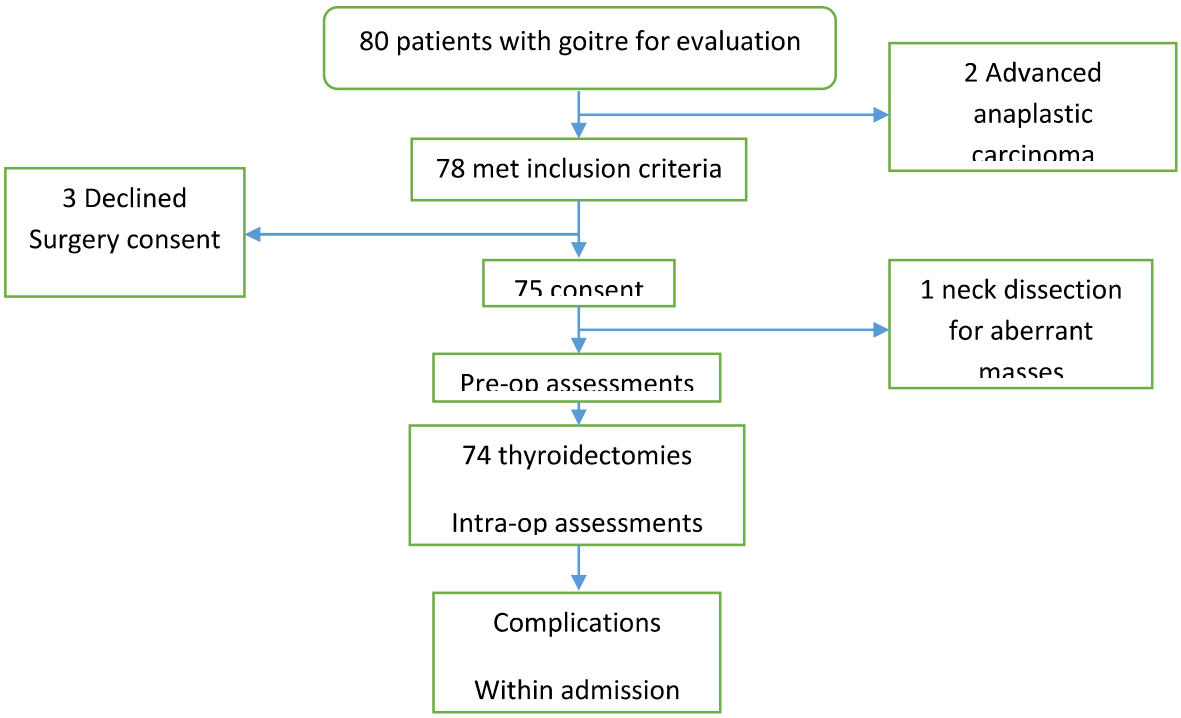

Figure 1: Enrolment Schema

Preoperative evaluation

Through history, clinical examination and select laboratory and radiological investigations, the following variables were documented. Demographic data collected included age, gender, ethnicity and place of residence. All patients had blood samples taken for a complete blood count, renal function tests and thyroid function tests i.e. TSH, T4 and T3. Patients who were found to have thyrotoxicosis were medically treated to a euthyroid state before they were offered surgery. Failed medical treatment was considered after six to eight weeks of medication i.e. thionamides, Lugol's iodine and beta blockers. No patient was put on radioactive iodine. Patients with failed medical treatment were temporarily stabilised with high dose steroids and beta blockers prior to surgery.

Goitre characteristics were assessed as follows. An initial clinical examination confirmed the presence of goitre with assignment of a WHO grade. A goitre was considered retrosternal if any portion of it was located below the thoracic inlet with the patient lying supine and the neck fully extended. Any nodularity detected by physical examination was confirmed by ultrasound. An ultrasound detected single nodule in association with hyperthyroidism was labelled "solitary toxic nodule". Hyperthyroidism with a diffuse swelling in association with opthalmopathy was labelled "Grave's disease". Multiple nodules in association with hyperthyroidism was labelled "Plummer's disease" Suspicious nodules were further evaluated by FNA.

Presence of dysphagia, dyspnoea, orthopnoea and voice changes i.e. hoarseness, fatigue, loss of range in association with a goitre were considered compressive symptoms. Preoperative hoarseness of voice was further evaluated by flexible endoscopic laryngoscopy by the ENT

surgeon to rule out vocal cord paralysis. Presence of comorbid medical conditions was also documented.

Intraoperative Evaluations

Duration of surgery was established as the time from skin incision to skin closure, measured in minutes. The category of surgeon conducting the thyroidectomy was noted i.e. General surgeon, ENT surgeon or resident. Surgery was conducted by the technique outlined earlier. "Extracapsular dissection" referred to the technique of hugging the thyroid capsule during the lateral component of dissection with the development of a plane between the capsule and the branches of the inferior thyroid artery. "Intra/subcapsular dissection" involved dissection at a plane medial to the thyroid capsule i.e. intraglandular. Whether or not the recurrent laryngeal nerves and the parathyroid glands were visualised was also noted. Finally, the extent of resection was noted. Intraoperative neural monitoring was not used. At extubation, the vocal cords were examined by direct laryngoscopy.

Hemostasis was achieved by combinations of suture ligature and electrosurgical energy device. Drain use was noted.

Postoperative evaluations

At the post anaesthesia care unit (PACU), standard postoperative monitoring was done. In addition, signs of bleeding from the wound, upper airway obstruction and thyroid storm were continually looked for. In order to detect airway obstruction, oxygen saturation and airway patency were continuously recorded. A stitch removing tray was maintained at the bed side and an emergency tracheostomy tray kept available. The wound dressing was inspected for signs of bleeding or oozing. The edge of the dressing was inspected for neck swelling as

indicated by a change in fit of dressing or neck circumference. Drainage from the glove drain was monitored by keeping a gauze count. Each piece of soaked gauze represented 20 -30 millilitres. Vigilance was kept high for signs and symptoms of thyroid crisis i.e. high temperature, high pulse rate, severe sweating and delirium.

Postoperative bleeding was defined as bleeding after wound closure that required surgical intervention due to: rapid accumulation of blood within the fascial-cutaneous layers surrounding the thyroid bed, more than 150mls estimated loss in the first 24 hours postoperatively and symptoms of airway obstruction. Postoperative bleeding estimated at between 50-100mls was designated as "significant". This was in line with studies which showed that bleeding >50mls was associated with increased risk of seroma and systemic complications of thyroid surgery(Simsek Celik et al., 2011). Evaluation for bleeding continued for the first 48 hours postoperative.

In the ward, daily clinical examinations were used to identify and document complications. Postoperative hypocalcaemia was defined as serum calcium <1.875mmol/L with clinical signs and symptoms. This serum cut-off level was chosen because it had been shown that below it, patients became symptomatic and needed treatment (Jessie & Harrison, 2010; A. R. Zambudio et al., 2004). Chvostek's and Trousseau's tests and perioral paraesthesia were used to screen for the presence or absence of hypocalcaemia. Patients who had these signs of hypocalcaemia had a serum calcium level determined. Vigil was kept high for other symptoms that generally indicate severe, life threatening hypocalcemia. These signs include tetany, laryngospasms, cardiac arrhythmias, cardiac arrest and neurological symptoms. All such patients were put on calcium and vitamin D supplements.

Recurrent laryngeal nerve palsy was defined as impaired vocal fold function in patients with normal preoperative function (Bures, Klatte, Friedrich, Kober, & Hermann, 2014). Gold standard for assessment was endoscopic naso-laryngoscopy. Indirect laryngoscopy use was limited by varying patient tolerance to gag reflex and limited view. Voice changes i.e. hoarseness and breathiness with weak cough, were used for screening despite known low sensitivity (33 – 68%) and positive predictive values of 38% (G. W. Randolph & Kamani, 2006). However, citing high rate of occurrence of voice changes in association with RLN palsy, there are local studies that support their use for screening in poor resource settings(Chalya et al., 2011; Wahome, 2007). All patients with voice hoarseness were followed up at 2 weeks and at 6 weeks at which point an endoscopic naso-laryngoscopy was done.

The surgical site was monitored for the presence of infection, seroma and flap edema. Infection was considered present by the occurrence of fever, localised neck pain, swelling around incision, odynophagia and a malodorous discharge. Presence of leucocytosis was helpful in establishing this diagnosis. Seroma was indicated by presence of an anterior neck swelling that issued a clear serous fluid on aspiration. Flap edema was considered present with the finding of skin flap puffiness and swelling located about 1-2cm from the incision site without infection. Thyroid Function tests were done at six weeks postoperative. This marked the end-point of the study.

Roles of the researcher

All data was collected by the researcher by the use of a clinical and biographic interviewer administered questionnaire. This included: preoperative, intraoperative and postoperative

clinical assessments and interpretation of laboratory test results; preoperative patient preparation; general postoperative management; management of complications.

3.7 Data processing and Analysis

The data was coded from pre-checked completed questionnaires, digitalized into a computer and analyzed using SPSS v. 21 analytical software (SPSS Inc., Chicago, Illinois). Access to the computer was limited by a password that was only known to the author.

Frequency tables were generated for categorical variables while means (standard deviations) were done for continuous variables.

The results were presented in form of tables, bar graphs and pie charts

Contingency tables with Fischer's exact and Student's t-tests (independent sample, two-tailed) were used to evaluate association between complications and multiple determinant factors in bivariate analysis. Statistical significance set at p-value <0.05

3.8 Study limitations

- Use of Chvostek's and Trousseau's signs to screen for hypocalcaemia and voice hoarseness for RLN injury may have led to under detection of their respective complications. To mitigate against this, final diagnosis was only made at end of study period after confirmation by serum calcium and endoscopic naso-laryngoscopy for hypocalcemia and RLN injuries respectively. These definitive evaluations were however only done to patients who were positively screened.

- Lack of radionuclide studies meant there may have been inaccuracies in the definitions of solitary toxic nodules, Grave's disease and Plummer's disease. This study relied on thyroid ultrasound.
- Assessment of surgeon factors was limited to their undergraduate and postgraduate degree qualification. This may not be an accurate measure of their proficiency in performing thyroidectomy
- Some intraoperative findings were not directly observed by the author. Accuracy of such observations was thus reliant on accurate record keeping by the operating surgeon.
- The fact that the author actively participated in the management of the patients may have introduced an observational bias when documenting the complications arising from his interventions.
- Low patient numbers prevented a multivariate analysis. Hence, confounders cannot be satisfactorily accounted for.

3.9 Ethical considerations

The author got ethical clearance from the Institutional research ethics committee (IREC) of Moi University to carry out this study. Approval no IREC 000876. Additionally, permission from MTRH administration was sought and granted before commencement of data collection.

The purpose of the study was explained to each participant in a language that they fully understood either by the author or through the employ of an interpreter. Informed consent was subsequently obtained from each participant.

For those below 18 years of age, consent was to be obtained from their parents or legal guardians. However, all the participants were 26 years and above. Confidentiality was maintained during and after the research. All records were kept under lock and key by the author.

All participants were assigned codes that de-identified them to avoid use of names

Participants were freely able to enter or leave the study at any point without undue pressure. Patients who declined to give consent for the study got standard care with no victimization. There were no financial inducements to participate in the study.

Results of the study were communicated back to the participants.

Primary data collection tools were shredded upon completion of study

4 Results

4.1 Demographic characteristics

Between August 2012 and August 2013, 74 thyroidectomies were performed. There were 73 females (98.6%) and 1 male (1.4%) with mean±SD age of 49.54±12.584 years. The age range was 26 – 88 years. Age distribution is as shown in figure 2 below:

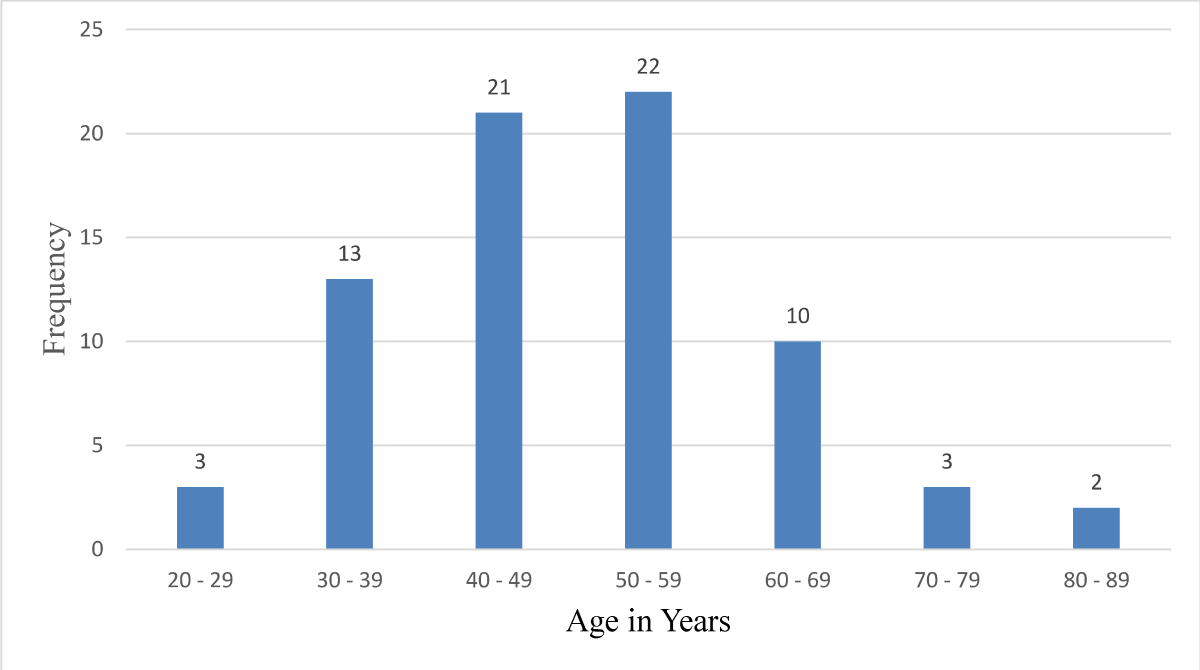

Figure 2: Age distribution of patients who underwent thyroidectomy

The most frequent age grouping was between 40 – 59 years. Further analysis showed that 95.9% (n = 71) of the participants were above the age of 30 years.

Most of the study participants reside in the highland and mountainous regions of the Rift valley province and its environs with altitudes generally above 1500 metres over sea level. These areas are rural and semi urban. The distribution of the resident districts mirrors the catchment area of the Moi Teaching and Referral Hospital. This is also reflected in the

cosmopolitan ethnic makeup albeit with a Kalenjin predominance. This is depicted in the tables 3 and 4 below:

Table 3**:** Tribal constitution of patients with goitres

Tribe	**Frequency**
Kalenjin	52 (70.3%)
Luhya	13 (17.6%)
Kikuyu	4 (5.4%)
Kisii	4 (5.4%)
Kamba	1 (1.4%)
Total	74 (100%)

Table 4**:** Geographical areas of residence of patients with goitres

County	**Frequency**
Uasin Gishu	25 (33.8%)
Nandi	14 (18.9%)
Elgeyo Marakwet	5 (6.8%)
Keiyo	5 (6.8%)
Wareng	5 (6.8%)
Vihiga	4 (5.4%)
Kapenguria	2 (2.7%)
Kakamega	2 (2.7%)
Trans Nzoia	2 (2.7%)
Kericho	2 (2.7%)
Njoro	1 (1.4%)
Nyeri	1 (1.4%)
Molo	1 (1.4%)
Lugari	1 (1.4%)
Nyamira	1 (1.4%)
Pokot	1 (1.4%)
Bungoma	1 (1.4%)
Siaya	1 (1.4%)
Total	**74 (100%)**

4.2 Goitre characteristics

A clinical diagnosis of a nontoxic multinodular goitre was made in 61 (82.43%) patients with 37 of them having bilateral involvement. Clinically diagnosed Grave's disease was found in 3 (4.05%) and solitary toxic nodule in 6 (8.11%) patients respectively. Simple diffuse goitres were found in 3 patients while only 1 had Plummer's disease. Table 5 illustrates this:

Table 5: Preoperative clinical diagnoses

Diagnosis	**Frequency**
nodular non-toxic bilateral	37 (50%)
nodular non-toxic unilateral	24 (32.4%)
toxic solitary nodule	6 (8.1%)
Diffuse toxic bilateral (grave's disease)	3 (4.1%)
diffuse non-toxic bilateral (Simple)	3 (4.1%)
nodular toxic bilateral (Plummer's disease)	1 (1.4%)
Total	**74 (100%)**

Ten patients were found to have hyperthyroidism by clinical symptoms and the finding of a serum TSH below 0.27mIU/ml. All but 3 had their symptoms well controlled with a combination of thionamides and beta blockers. None of them were on steroids or radioactive iodine. For those patients with uncontrolled disease, two had Grave's disease and one had a

solitary toxic nodule. One patient whose histology was reported as multinodular goitre had a low TSH but this was explained by her taking of suppressive levothyroxine doses preoperatively. There was only one case of Plummer's disease. All in all, 91.8% (n = 68) of patients were euthyroid at presentation. Preoperative TFTs are illustrated in the figure below:

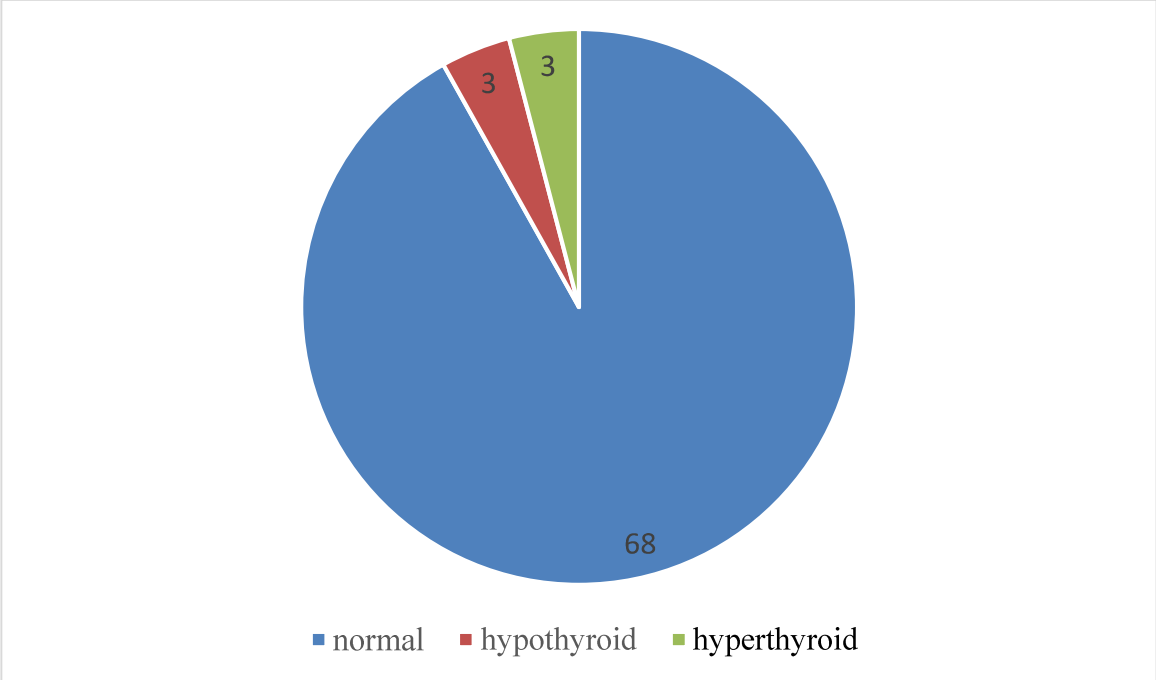

Figure 3: Preoperative Thyroid Function Tests

Three patients presented with hypothyroidism. In one, this was ascribed to an underlying Hashimoto's thyroiditis while the other two patients had large multinodular colloid goitres with cystic degeneration. Both were on an erroneous prescription of carbimazole from another health facility.

Out of the 74 study participants, 48 (64.86) had an FNAC done. Selection was largely based on the clinical judgement of the attending surgeon. All were done without ultrasound

guidance. A preoperative diagnosis of benign or malignant goitre was made in 45 (93.75%) and 3 (6.25%) patients respectively. Other diagnoses were distributed as depicted in table 6 below.

Table 6: Preoperative FNAC diagnoses

Diagnosis	**Frequency**
Colloid goitre	37 (77.1%)
Thyroiditis	4 (8.3%)
Thyroid cyst	2 (4.2%)
Follicular Carcinoma	2 (4.2%)
Thyroid adenoma	1 (2.1%)
Cystic degenerative	1 (2.1%)
Colloid goitre carcinoma	1 (2.1%)
Total	**48 (100%)**

Histology was considered the gold standard of examination. All patients had a histological examination of their thyroidectomy specimen. Multinodular colloid goitres comprised 85% (n=63) of all specimen. Only one diagnosis of follicular carcinoma was made by histology. There were no cases of papillary, hurthle cell, anaplastic or medullary carcinomas. None of the FNAC diagnoses of malignancy were confirmed by histology. Histological examination

revealed them to be colloid goitres. Similarly, of the four FNAC diagnoses of thyroiditis, histology could only confirm two.

Table 7 below shows Histological diagnoses. Comparison of FNAC and Histological examinations is depicted in Table 8.

Table 7: Histological diagnosis of patients with goitre

	Frequency	Percent
follicular adenoma	1	1.4
follicular carcinoma	1	1.4
multinodular goitre	57	77.0
Hashimoto's thyroiditis	2	2.7
follicular adenoma & multinodular goitre	7	9.5
cystic degeneration & multinodular goitre	6	8.1
Total	74	100.0

Table 8: Comparison of FNAC versus Histology

FNAC	Histology					Total
	Follicular carcinoma	Multinodular goitre	Hashimoto's thyroiditis	Follicular adenoma & multinodular goitre	Cystic degeneration & multinodular goitre	
Colloid goitre	1	31	0	2	3	37
Thyroid adenoma	0	0	0	1	0	1
Thyroid carcinoma	0	2	0	0	0	2
Thyroiditis	0	2	2	0	0	4
Cystic degenaration	0	1	0	0	0	1
Thyroid cyst	0	0	0	1	1	2
Colloid goitre with carcinoma	0	1	0	0	0	1
	1	37	2	4	4	48

Shaded areas show agreement between FNAC and histology

Equivalence of histological and FNAC diagnoses is as shown below:

Colloid Goitre = multinodular goitre

Thyroid adenoma = follicular Adenoma

Thyroid carcinoma = follicular carcinoma

Thyroiditis = Hashimoto's thyroiditis

Cystic degeneration and Thyroid cyst = cystic degeneration

With Histology being the gold standard, calculation of sensitivity, specificity, positive and negative predictive values is as shown below:

Table 9**:** Sensitivity of FNAC

		Histology		
		Yes	No	Total
FNAC	Yes	41	7	46
	No	53	187	240
	Total	94	194	288

Sensitivity = 43.6%

Specificity = 96.4%

Positive predictive value = 89.1%

Negative predictive value = 77.9%

Choice and extent of surgery was partially determined by the preoperative diagnosis. This was especially so with FNAC diagnoses of malignancy and/or thyroiditis where there was a tendency to perform more extensive resections (Total and Near Total thyroidectomies). Table 10 explores this relationship.

Goitres were assessed and graded according to the 1986 WHO classification. There were 40 (54.05%) grade III, 31 (41.89%) grade II and 3 (4.06%) grade I goitres. Six patients (8.1%) were found to have a retrosternal extension of their goitres. Their main complaints and

indications for surgery were equally split between compressive and cosmetic concerns. All of them had grade II and III size goitres that were benign. None had superior vena cava syndrome or a positive Pemberton's sign.

Table 10**:** Effect of FNAC diagnosis on the extent of surgery

FNAC	**Extent of Surgery**								Total
	TT	ST	NTT	LOB	PLOB	DP	HT	NTT & PI	
Colloid Goitre	2	9	2	5	7	6	5	1	37
Thyroid adenoma	0	0	0	0	1	0	0	0	1
Thyroid carcinoma	1	0	1	0	0	0	0	0	2
Thyroiditis	0	2	2	0	0	0	0	0	4
Cystic degeneration	0	0	0	0	1	0	0	0	1
Thyroid cyst	0	0	0	2	0	0	0	0	2
Colloid goitre with carcinoma	1	0	0	0	0	0	0	0	1
Total	4	11	5	7	9	6	5	1	48

TT – total thyroidectomy; ST – subtotal thyroidectomy; NTT – near total thyroidectomy; LOB – lobectomy; PLOB – partial lobectomy; DP – Dunhill procedure; HT – hemithyroidectomy; PI – parathyroid implantation.

Sixty (81.08%) patients complained of compressive symptoms involving the upper aero digestive tract. The remaining 14 patients were largely asymptomatic with most having cosmetic concerns or minor discomfort in the neck. No patient presented with a goitre recurrence. Four patients had minor dysphonic symptoms preoperatively. They were all

determined to have mild laryngitis by ENT evaluation. No preoperative nerve palsies secondary to goitre compression were evident.

4.3 Indications for surgery

The general indications for surgery are given below:

Table 11**:** Indications for Surgery

Indication	**Frequency**
Suspected malignancy	3 (4.1%)
Compressive symptoms	58 (78.4%)
Cosmesis	10 (13.5%)
Failed medical treatment	3 (4.0%)
Total	74 (100%)

There were no operations for goitre recurrence after a previous partial resection.

4.4 Early postoperative complications

4.4.1 Factors determining complications (Hypothesized causal variables)

Comorbidities

Comorbid diseases were found in 26 (35.1%) patients. All were well controlled prior to surgery. Hypertension and related complications affected 16 patients with three of them having concurrent diabetes mellitus. None of the patients had known neurological or

psychiatric illnesses that affected speech quality. Three patients were HIV positive while the rest had miscellaneous conditions e.g. medically well controlled epilepsy, gastritis. There were no coagulopathies and none of the patients were on lithium or amiodarone that are known to affect thyroid function. None of the patients were pregnant. All the patients had normal preoperative complete blood counts and kidney function tests.

Surgeon specialisation

Surgery was conducted by either general surgeons, ENT surgeons or registrars largely under the supervision of the general surgeons. All registrars had at least five years of practice in general surgery. Table 12 summarises this

Table 12: Surgeon specialisation

	Frequency
Registrar	4 (5.4%)
General surgeon	60 (81.1%)
Ear, Nose and throat surgeon	10 (13.5%)
Total	74 (100%)

Type/Extent of thyroidectomy

Type and extent of thyroidectomy procedure were determined by the preoperative diagnosis and surgeon's intraoperative judgement. Overall, there were 40 (54.05%) bilateral procedures and 34 (45.95%) unilateral ones. Taken singly, subtotal thyroidectomy was most

common. There were no neck dissections done in this study. The range of procedures done is depicted in Table 13 below.

Table 13**:** Type/extent of thyroidectomy procedures

	Frequency
Total thyroidectomy	4 (5.4%)
Subtotal thyroidectomy	21 (28.4%)
Near total thyroidectomy	6 (8.1%)
Lobectomy	16 (21.6%)
Partial lobectomy	11 (14.9%)
Dunhill procedure	8 (10.8%)
Hemi thyroidectomy	7 (9.5%)
Near total thyroidectomy with parathyroid implantation	1 (1.4%)
Total	**74 (100%)**

The mean±SD duration of surgery was 98.84±46.785 minutes with the longest and shortest surgeries taking 260 and 20 minutes respectively. Most surgeries took 60 minutes. The mean±SD duration of hospital stay after operation was 3.12±1.565 days with a range of 1- 8 days.

Patients' data on the indications for surgery, duration of surgery, and length of hospital stay are summarized in Table 14.

Table 14**:** Clinical summary

Clinical diagnosis	N	Mean hospital stay (days)	Mean op time (min)
Nodular non-toxic bilateral	37	3.24	104.41
Nodular non-toxic unilateral	24	2.82	82.33
Nodular toxic bilateral	1	2.00	90.00
Diffuse toxic bilateral	3	2.67	106.67
Toxic solitary nodule	6	3.00	67.33
Diffuse non-toxic bilateral	3	5.00	121.67
Total	74	3.12	94.84

Technique/type of dissection

Intracapsular (also called subcapsular) dissection was used in 44 (59.5%) patients, all involving variants of partial gland resections. The rest, 30 (40.5%), had extracapsular dissections. Analysis of dissection type by surgeon is given in Table 13 below. Extracapsular dissection was practiced by 90% (n=9) of ENT surgeons while only 35% (n=21) of general surgeons did. The registrars used the intracapsular dissection type.

Table 15: Technique/type of dissection analysed by surgeon

		surgeon			Total
		registrar	gen surg	ent	
type of dissection	Extra - capsular	0	21	9	30
	Intra - capsular	3	38	1	42
	both	1	1	0	2
Total		4	60	10	74

The recurrent laryngeal nerves were visually identified only in 25 (33.8%) patients. There was a tendency to stay away from the nerves rather than visualise and protect them by 66.2% (n=49) of surgeons. Similarly, parathyroid glands were visualised in only 27 (36.5%) patients. Consequently, there was only 1 case of parathyroid auto transplantation.

All but 4 patients had passive rubber glove drainage of their thyroidectomy wounds.

4.4.2 Early postoperative complications and their determinants

Recurrent Laryngeal nerve palsy

All patients had subjective clinical voice assessment for dysphonia pre and postoperatively. Four patients had a preoperative laryngoscopy. At extubation, only 29 (39.2%) patients were assessed by laryngoscopy. At six weeks, 12 (16.2%) patients had a laryngoscopy that was based on their presentation with persistent hoarseness of voice.

Preoperative voice hoarseness was found in four patients. Direct laryngoscopy showed normal vocal cord movement in all of them. ENT diagnosis was mild laryngitis in all four. At extubation, 23 (31.1%) patients had voice hoarseness while 51 (68.9%) did not. Laryngoscopy could only confirm four abnormal vocal cord movements. There were three right recurrent laryngeal nerve palsies and one left. One of these patients had in addition a supraglottic oedema that necessitated endotracheal re-intubation and high dose steroids. None of the patients had bilateral paralysis.

At six weeks follow up, 12 patients presented with voice hoarseness. This included the four patients that had been picked by laryngoscopy at extubation. These patients still had nerve palsies. One additional patient presented with loss of voice power especially at high notes. Laryngoscopy showed slight bowing of his right vocal cord with sluggish movements suggestive of a palsy of the external branch of the superior laryngeal nerve. All the other seven patients had normal vocal cord movements. Cause of hoarseness was inflammatory changes around the glottis.

The rate of recurrent laryngeal nerve palsy at the end of the study was **5.4% (n=4)**. Palsy of the superior laryngeal nerve stood at **1.4% (n=1).**

The only factors favouring appearance of laryngeal nerve injuries by bivariate analysis were the extent of thyroidectomy ($p = 0.001$) and a preoperative FNAC diagnosis of carcinoma ($p = 0.008$). Visualisation of the recurrent laryngeal nerves during dissection was notably not significantly associated with recurrent laryngeal nerve palsy ($p = 0.328$). Out of the 25 operations in which the nerve was identified, 13% (n=3) had nerve palsy compared to only 4.3% (n=2) of the 49 operations in which the nerve wasn't identified.

Table 16**:** Variables associated with postoperative Laryngeal nerve injury: Bivariate analysis.

Variable	LNI	No LNI	P value
Age*	45.4±9.2	49.8±12.8	0.450
Compression SS			
No	0	14	0.576
Yes	5	55	
Retrosternal Goitre			
No	5	63	NS
Yes	0	6	
Goitre grade			
II	2	32	NS
III	3	37	
Duration of Surgery*	128±81.6	92.4±43.3	0.101
Comorbidity			
No	3	45	NS
Yes	2	24	
FNAC Thyroiditis			
No	3	41	NS
Yes	0	4	
FNAC Carcinoma			
No	1	44	**0.008**
Yes	2	1	
Extent of resection			
TT	3	1	**0.001**
STT	1	28	
NT	0	7	
LOB	1	26	
HT	0	7	
Dissection Type			
Extracapsular	3	27	0.69
Intracapsular	2	42	
Surgeon			
Gen Surgeon	5	59	NS
ENT	0	10	
RLN Visualized			
No	2	47	**0.328**
Yes	3	22	

'*' Data expressed as mean±SD; LNI – Laryngeal nerve injury; TT – total thyroidectomy; STT – subtotal thyroidectomy; LOB – lobectomy; HT – hemithyroidectomy; SS – signs and symptoms; NS – not significant

Hypoparathyroidism

All patients had clinical assessments for signs and symptoms of hypocalcemia. Serum calcium was done for symptomatic patients. Nonetheless, 39 (52.7%) patients had serum calcium done. Selection was additionally based on patients having undergone bilateral thyroid procedures that put all parathyroid glands at risk. This is shown in Figure 4 below:

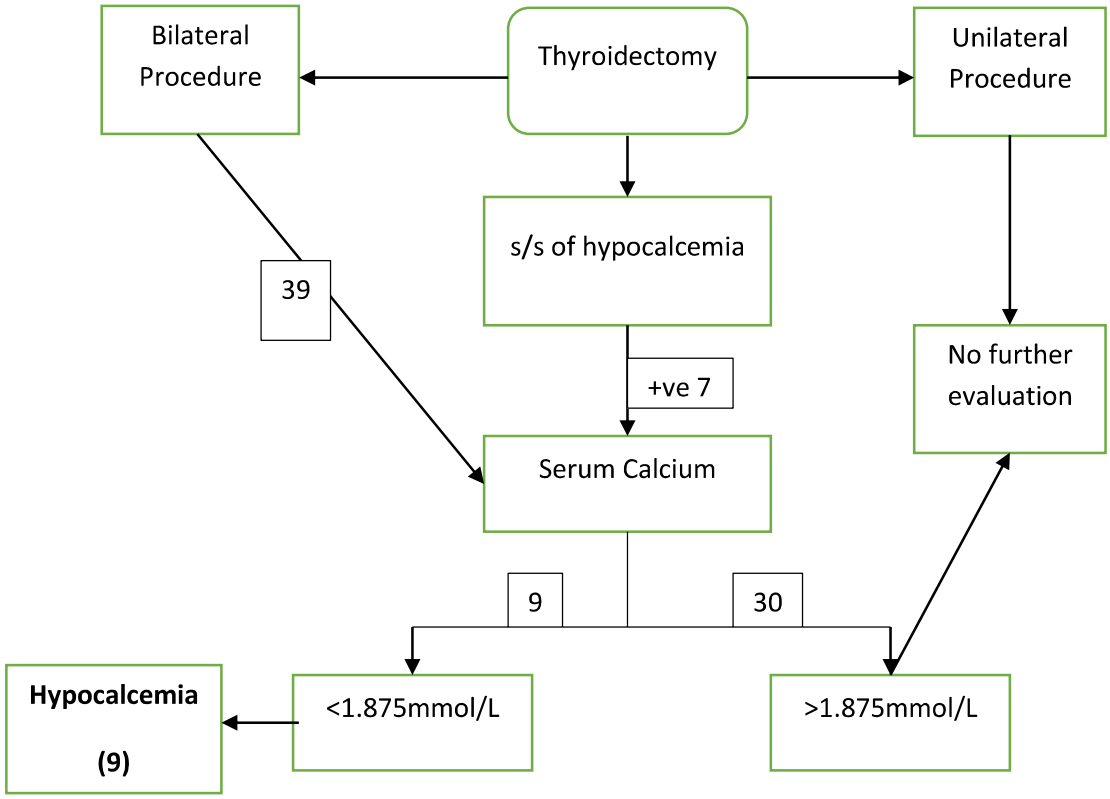

Figure 4:Hypocalcemia – patient flow

Table 17: Postoperative Serum calcium levels

	Frequency
Normalcalcemia	30 (76.9%)
Hypocalcemia	9 (23.1%)
Total	39 (100%)

It was noted that none of the patients had symptoms with serum calcium levels above 1.875mmol/L (7.5mg/dl). Nine (12.2%) patients presented with calcium levels below 1.875mmol/L with mean±SD of 1.80±0.09 mmol/L. Seven of these patients had signs and symptoms. Their mean±SD calcium levels were 1.79±0.10 mmol/L.

Table 18: Assessment of postoperative hypocalcemia by Chvostek's test

	Frequency
No	72 (97.3%)
Yes	2 (2.7%)
Total	74 (100%)

Table 19: Assessment of postoperative hypocalcemia by Trousseau's sign

	Frequency
No	69 (93.2%)
Yes	5 (6.8%)
Total	74 (100%)

Risk factors for the development of post-operative hypocalcemia were the **extent of resection** (p = 0.001), **FNAC diagnosis of carcinoma** (p = 0.038) and **dissection type** (p = 0.033). Extensive resections i.e. total and near total thyroidectomies, conferred higher risk for the development of postoperative hypocalcemia. An FNAC carcinoma diagnosis was similarly associated with higher risk.

Extracapsular dissection was associated with higher risk of postoperative hypocalcemia compared to intracapsular dissection. Out of the 30 extracapsular dissections done, 20% (n=6) had postoperative hypocalcemia. In comparison, only 6.8% of the 44 intracapsular dissections developed this complication. Of the 9 patients with hypocalcemia, 7 had extracapsular dissections yet it was only in 3 that the parathyroid glands were visualised. None of these patients had parathyroid gland auto transplantation.

All nine patients were put on a combination of vitamin D3 and calcium supplements. Next follow up was scheduled at three months. The hypocalcemia rate at the end of the study period was **12.2% (n = 9)**.

Presence of comorbid conditions, though not reaching statistical significance (p=0.059), showed a trend towards an association with postoperative hypocalcemia.

Table 20**: Variables associated with postoperative Hypocalcemia: Bivariate analysis**

Variable	Hypocalcemia (n = 9)	No Hypocalcemia (n=30)	P value
Age*	46.4±10.9	50±12.8	0.435
Compression SS			
No	2	12	0.676
Yes	7	53	
Retrosternal Goitre			
No	7	61	0.153
Yes	2	4	
Goitre grade			
I	0	3	NS
II	4	27	
III	5	35	
Comorbidity			
No	3	45	**0.059**
Yes	6	20	
FNAC Thyroiditis			
No	5	39	0.425
Yes	1	3	
FNAC Carcinoma			
No	4	41	**0.038**
Yes	2	1	
Extent of resection			
TT	2	2	**0.001**
STT	2	27	
NTT	4	3	
LOB	1	26	
HT	0	7	
Dissection Type			
Extracapsular	6	24	**0.033**
Intracapsular	3	41	
Surgeon			
Gen Sur	9	55	0.347
ENT	0	10	
PTG Visualized			
No	6	41	NS
Yes	3	24	
Postop stay *	3.56±2.2	3.06±1.5	0.374

'*' Data expressed as mean±SD; PTG – parathyroid gland; TT – total thyroidectomy; STT – subtotal thyroidectomy; LOB – lobectomy; NTT – near total thyroidectomy; HT – hemithyroidectomy; NS – not significant.

Post – operative bleeding.

Significant postoperative bleeding occurred in 7 (9.5%) patients. However it was only in 2 (**2.7**%) patients that there was an associated anterior neck hematoma necessitating emergency surgical exploration. This occurred despite use of surgical drains. These patients had compromised airways that became evident within 12hrs of operation. One patient's blood loss was severe enough to cause hypotension and require a blood transfusion during reoperation. Five patients that had wound drainage estimated at 50 – 100mls of blood in the first 24 hrs were managed expectantly. Three of them later developed seromas. In addition, one had a surgical site infection.

A summary of the two cases particularly emphasizing the fact that they were all grade III goitres with no other risk factors is given in the table below:

Table 21**:** Summary of two patients with postoperative bleeding

Variable	**Case 1**	**Case 2**
Age	63	42
Sex	Female	Female
Compressive symptoms	Yes	Yes
Goitre grade	III	III
Retrosternal involvement	No	No
Duration of surgery *	60	140
Comorbidity	No	No
diagnosis	Multinodular colloid	Multinodular colloid
Thyroiditis	No	No
Extent of resection	Subtotal	Hemi thyroidectomy
Surgeon	General Surgeon	ENT surgeon
'*' duration given in minutes		

Analysis of all seven cases with significant postoperative bleeding is shown in the table below.

Table 22: Variables associated with "significant" postoperative postop bleeding

Variable	Bleeding	No Bleeding	P value
Age*	52.6±14.0	49.2±12.5	0.507
Compression SS			
No	0	14	0.334
Yes	7	53	
Retrosternal Goitre			
No	6	62	0.461
Yes	1	5	
Goitre grade			
I	0	3	0.210
II	1	30	
III	6	34	
Comorbidity			
No	4	44	0.691
Yes	3	23	
Thyroiditis			
No	4	40	0.366
Yes	1	3	
Carcinoma			
No	5	40	NS
Yes	0	3	
Extent of resection			
TT	1	3	0.100
STT	4	25	
NTT	1	6	
LOB	0	27	
HT	1	6	
Surgeon			
Gen Sur	6	58	NS
ENT	1	9	
PTG Visualized			
No	4	43	0.701
Yes	3	24	
Postoperative stay *	4.9±1.6	2.9±1.5	**0.002**

'*' Data expressed as mean±SD; PTG – parathyroid gland; TT – total thyroidectomy; STT – subtotal thyroidectomy; LOB – lobectomy; NTT – near total thyroidectomy; HT – hemithyroidectomy; NS – not significant

From the analysis above, it can be seen that no factor was identified as being significantly associated with occurrence of postoperative bleeding. It was however noted that surgeries complicated by bleeding resulted in longer postoperative length of stay (p = 0.002).

Thus, using the two patients that needed exploration, the rate of postoperative bleeding was set at **2.7%** in this study. Bivariate analysis could not be done due to the low numbers.

Seroma formation

Postoperative anterior neck swelling with aspiration of clear fluid occurred in 6 (**8.1**%) patients. These patients had histological diagnoses of multinodular goitre which were clinically sized at grade II and III. There were two total thyroidectomies, two subtotal thyroidectomies, one hemi thyroidectomy and one partial lobectomy procedures done. Diabetes mellitus and HIV were the featured comorbid conditions in two patients. Three patients had associated surgical site infections. There was no association of statistical significance when seroma formation was analysed by **extent of resection** (p = 0.71). However, surgeries complicated by seroma formation lasted longer than those without this complication i.e. mean±SD of 136±65.3 minutes versus 91.1±43.5 minutes. This difference reached statistical significance (p = 0.021).

Infection

Superficial surgical site infection was found in 3 (**4.1%**) of cases. These were females, above sixty years old and with benign multinodular goitres. One had diabetes mellitus. During admission, they all had postoperative seroma diagnosed.

Table 23: Variables associated with postoperative seroma: Bivariate analysis

Variable	Seroma	No Seroma	P value
Age*	56.2±18.9	49±11.9	0.180
Compression SS			
No	0	14	0.587
Yes	6	54	
Retrosternal Goitre			
No	5	63	0.409
Yes	1	5	
Goitre grade			
I	0	3	0.398
II	1	30	
III	5	35	
Comorbidity			
No	4	44	NS
Yes	2	24	
Thyroiditis			
No	4	40	
Yes	0	4	NS
Carcinoma			
No	3	42	0.234
Yes	1	2	
Extent of resection			
TT	2	2	0.71
STT	2	27	
NTT	0	7	
LOB	1	26	
HT	1	6	
Surgeon			
Gen Sur	6	58	0.588
ENT	0	10	
Postop stay *	4.3±2.2	3±1.5	0.213
Duration of surgery	136±65.3	91±43.5	**0.021**

'*' Data expressed as mean±SD; TT – total thyroidectomy; STT – subtotal thyroidectomy; LOB – lobectomy; NTT – near total thyroidectomy; HT – hemithyroidectomy.

Symptoms of fever, neck pain and swelling, minor dysphagia and a thin discharge from the surgical site were evident within one week. The patient with diabetes was hospitalised for one week due to the need for intravenous medications and blood sugar control. The other

patients presented at the surgical outpatient clinic within five days of discharge. They were all managed with a combination of antibiotics and dressing changes.

The only risk factors identified by bivariate analysis was **age (p = 0.001).**

Table 24: Variables associated with surgical site infection: Bivariate analysis

Variable	**Infection**	**No Infection**	**P value**
Age*	71.7 ±9.7	48.6 ±11.9	**0.001**
Compression			
No	0	14	NS
Yes	3	57	
Retrosternal Goitre			
No	3	65	NS
Yes	0	6	
Goitre grade			
II	1	30	NS
III	2	38	
Duration of Surgery*	103.3 ±32.1	94.5 ±47.4	0.751
Duration of Hosp. stay*	4 ±2.6	3.1 ±1.5	0.322
Comorbidity			
No	2	46	NS
Yes	1	25	
FNAC Thyroiditis			
No	2	42	NS
Yes	0	4	
FNAC Carcinoma			
No	2	43	NS
Yes	0	3	
Extent of resection			
TT	0	4	0.674
STT	1	28	
NTT	0	7	
LOB	1	26	
HT	1	6	
Surgeon			
Gen Sur	2	58	NS
ENT	0	10	

Flap oedema

Flap oedema complicated **6.8%** (n=5) of thyroidectomies. All patients had benign nodular grade III sized goitres. Surgery was performed for compressive symptoms by all categories of surgeons. No risk factor was identified in this study by bivariate analysis

Table 25: Presence of flap oedema

	Frequency
No	69 (93.2%)
Yes	5 (6.8%)
Total	74 (100%)

Airway obstruction

Three patients (**4.1%**) presented with a compromised airway postoperatively. Two had suffocating hematomas due to reactionary haemorrhage. The third patient had a unilateral vocal cord palsy in addition to supraglottic oedema. All the serum calcium levels were normal. Risk analysis was not done because there were only 3 cases

Hypothyroidism

All the four cases of total and five of near total thyroidectomy had levothyroxine supplementation with or without postoperative TFTs. Only 20 (27%) patients had postoperative TFTs done. All patients were assessed clinically for signs and symptoms of hypothyroidism. Out of the 20 with TFTs, there were 6 (**33%**) cases of biochemical

hypothyroidism. Two patients had a preoperative diagnosis of Hashimoto's thyroiditis with one of them presenting with hypothyroidism. The other 4 patients had multinodular colloid goitres. There were two operations each distributed evenly amongst total, near total and subtotal thyroidectomies. Association between extent of thyroidectomy and hypothyroidism did not reach statistical significance (p=0.454). Similarly, association between thyroiditis and hypothyroidism did not reach statistical significance (p = 0.214). Hypothyroidism in this study seemed to represent inadequate dosage of levothyroxine.

4.4.3 Overall complication and the extent of thyroidectomy

Table 26: Association between extent of surgery and overall complication

	Complication		Total	
	no	yes		p-value
Total thyroidectomy	0	4	4	**<0.001**
Subtotal thyroidectomy	18	11	29	
Near total thyroidectomy	2	5	7	
Lobectomy	24	3	27	
Hemi thyroidectomy	5	2	7	
Total	49	25	74	

Above table shows significant clustering of complications when distributed amongst the various types of resection. Extensive resections had more complications.

Table 27: Association between surgeon and overall complication

	complication		Total	
	no	yes		p-value
General surgeon	38	22	60	**0.476**
Ear, Nose and Throat surgeon	8	2	10	
Total	46	24	70	

From above table, it can be seen that while only 20% (2/10) of procedures done by ENT surgeons had complications, the corresponding figure for the general surgeons was 36.7% (22/60). This difference did not reach statistical significance (p = 0.476).

A summary of the distribution of early postoperative complication by the extent of surgery is given in the table below:

Table 28: Analysis of early postoperative complications by extent of surgery.

	type of thyroidectomy								Total	p-value
	TT	STT	NTT	LOB	PLOB	DP	HT	NTT n PI		
flap edema	0	2	1	0	1	1	0	0	5	0.642
seroma	2	2	0	0	1	0	1	0	6	0.124
airway compromise	0	2	0	0	0	0	1	0	3	0.628
infection	0	1	0	0	1	0	1	0	3	0.653
hypothyroid	2	2	2	0	0	0	0	0	6	0.454
RLNP	3	1	0	1	0	0	0	0	5	0.030
hypocalcemia	2	0	4	1	0	2	0	0	9	0.002
bleeding	0	1	0	0	0	0	1	0	2	0.585
Total	**9**	**11**	**7**	**2**	**3**	**3**	**4**	**0**	**39**	

TT – total thyroidectomy; STT – subtotal thyroidectomy; NTT – Near total thyroidectomy; LOB – lobectomy; PLOB – partial lobectomy; DP – Dunhill procedure; HT – Hemi thyroidectomy.

In summary, the table above shows that Recurrent laryngeal nerve palsy and hypocalcemia rate was significantly associated with the type of resection. The extensive resections were associated with a higher number of these two complications.

4.4.4 Summary of complications and their determinants

Thirty-nine complications occurred in 25 (33.8%) patients corresponding to 5 laryngeal nerve injuries, 9 hypocalcemia, 2 postoperative bleeds, 3 airway obstructions, 6 seroma, 5 flap oedema, 3 surgical site infections and 6 hypothyroidism. There were no mortalities or thyrotoxic crises. Age (Mean±SD) for patients with complications was 50.4±12.1 vs 49.1±12.9 years for those without. This difference was statistically insignificant (p = 0.358). The mean±SD postop stay was 3.9±2.1 days for patients with complications vs 2.7±1.0 days for those without. i.e. patients with complications had a longer convalescence (p = 0.014).

After bivariate analysis, the risk factors for development of postoperative complications were **Extent of resection** (p = <0.001), **FNAC diagnosis of carcinoma** (p = 0.026) and FNAC diagnosis of **Thyroiditis** (p = 0.007). It was noted that postoperative complications led to a longer convalescence – **postoperative stay** (p = 0.014), and the surgeries took longer to perform – **duration of surgery** (p = <0.001). Surgeon specialisation, presence of compressive symptoms, grade of goitre and retrosternal extension of goitre were not independent risk factors for complications. Multivariate analysis was not possible due to the low number of participants

Table 29: Variables associated with postoperative complication: Bivariate analysis

variables	Complication (n =25)	No complication (n =49)	P value
Age	50.4±12.1	49.1±12.9	0.664
Compression SS	21	39	0.769
Goitre grade			
I	0	3	0.323
II	9	22	
III	16	24	
Duration of surgery	122.2±51.8	80.9±37.4	**<0.001**
Comorbidity	11	15	0.254
Retrosternal goitre	4	2	0.171
FNAC thyroiditis			
Yes	4	0	**0.007**
No	11	33	
FNAC carcinoma			
Yes	3	0	**0.026**
No	12	33	
Extent of resection*	25	49	**<0.001**
Surgeon**	24	46	0.476
Post op stay	3.9±2.1	2.7±1.0	**0.014**
Dissection Type			
Extracapsular	13	17	0.211
Intracapsular	12	32	

'*' refers to total vs subtotal vs near total vs lobectomy vs hemi thyroidectomy;
'' refers to General surgeon vs ENT surgeon vs Registrar**

5 Discussion

5.1 Demographics

The female to male ratio in this study was five to thirty times more than comparable national (Wagana, Mwangi, Bird, & Hill, 2002) and regional studies that had ratios between 15:1 and 5:2(Abebe et al., 2007; Chalya et al., 2011; Dakubo, Naaeder, Tettey, & Gyasi, 2013; Idris, Ali, & Hamza; Kpolugbo, Uhumwangho, Obasikene, & Alili, 2013; Mohamed, Abakar, & Bakhiet, 2009). The mean age of 49.54±12.584 years was ten to twenty years higher than the average ages quoted in regional studies. This, however, was similar to studies from the western world (Avenia et al., 2009; G. Dionigi, Rovera, Boni, & Dionigi, 2008; Karamanakos et al., 2010; A. R. Zambudio et al., 2004). One possible explanation to this lies in the effect of successful dietary iodine supplementation on the epidemiology of iodine deficient goitres. Iodine deficiency, as measured by median urinary iodine concentration, has a prevalence of 42% in Africa (Ogbera & Kuku, 2011; Smyth, 2014). In iodine deficient populations, like Kenya was prior to 1970, there is a predisposition to thyroid enlargement during periods of enhanced requirements of thyroid hormone i.e. puberty, pregnancy and physiological lactation. Females are additionally susceptible due to hyperestrogenism (Lewinski, 2002). Thus, without iodine supplementation, goitres will generally be observed in children and women of child-bearing age. With supplementation, females of older age groups will be affected. The current study is reflective of this. Prior to 1990 (before the World Summit for Children), there were no comprehensive iodine supplementation programmes in most African countries. Kenya, in contrast to its neighbouring countries had its programme rolled out in 1970 (Wagana et al., 2002). Currently, Kenya is classified by

UNICEF as iodine sufficient, similar to most western nations (Jooste, Andersson, & Assey, 2014).

The Kalenjin made up 70.3% of the respondents. This was probably due to the fact that MTRH is located in Uasin Gishu County, a region largely inhabited by the Kalenjin tribe. The hospital serves as a primary surgical care facility for the surrounding communities in addition to being Kenya's second national referral hospital. The respondents' districts of residence reflected the catchment area of MTRH. These areas are mostly rainy, hilly, mountainous, and rural to semi – urban. They were traditionally part of the endemic goitre belt of Eastern Africa prior to salt iodisation programmes (Davies, 1994; Hanegraaf & McGill, 1970; Kelly & Snedden, 1958). It is of interest that although dietary iodine supplementation is considered adequate in these areas, goitres still cluster here. This discrepancy between goitre rates and iodine dietary consumption implies contribution of additional factors in goitre development (Smyth, 2014). These factors may include consumption of dietary goitrogens e.g. thiocyanates which are found in cassava, millet, kale, cabbages and sweet potatoes. Others include selenium, iron and vitamin A deficiency.

5.2 Goitre characteristics

Eighty five percent of goitres operated on were benign and multinodular and represented the commonest mode of presentation. Over half of these goitres were WHO grade III. Most regional studies agree with this finding (Abebe et al., 2007; Chalya et al., 2011; Mohamed et al., 2009). It is known that pathological forms of goitre in endemic areas conform to a defined pattern with large hyperplastic or colloid goitres being the commonest histological type (>70%) (Acun et al., 2004). Consequent to this, the most common indication for surgery in this study and others regionally was the presence of compressive symptoms.

The rate of preoperative hyperthyroidism in this study was similar to a 2004 study by Hill et al at Kijabe Mission Hospital which found a rate of 13% (Hill et al., 2004). Fualal et al in Uganda found a rate of 15% (Fualal et al., 2012). However, these rates were two to three times higher than reported rates from the Sudan – 6.5%(Mohamed et al., 2009), Ethiopia – 3.6%(Abebe et al., 2007) and Tanzania – 7.9% (Chalya et al., 2011). These latter rates compare favourably with older Kenyan series by Kung'u and Adwok in 1974 and 1995 respectively (Adwok, 1995; Kung'u, 1974). The current high rates of hyperthyroidism may indicate better iodine nutrition status in Kenya and Uganda compared to the other countries in the region. Iodine induced thyrotoxicosis due to supplementation in the setting of long standing single or multiple thyroid nodules in chronically iodine deficient patients has been observed in Zimbabwe (Todd et al., 1995) and Zaire (Bourdoux, Ermans, wa Mukalay, Filetti, & Vigneri, 1996). It has been postulated that these high rates may reflect conversion of non-functional thyroid nodules to a hyper functioning state with supplementation (Jod-Basedow effect). This may represent the transition from iodine deficient to iodine sufficient, or excess states. Autonomously functioning thyroid nodules could also explain this rate (Fualal et al., 2012).

The rate of malignancy and thyroiditis in the current study was five to ten times lower than other national (Adwok, 1995; Kung'u, 1974; Wagana et al., 2002) and regional studies (Bakheit, Seif, & Mohamed, 2008; Dakubo et al., 2013; Mohamed et al., 2009). These studies also showed a higher incidence of papillary compared to follicular thyroid carcinomas. In these studies, Grave's disease also featured prominently in comparison to Hashimoto's thyroiditis unlike the current study. Studies from outside Africa further illustrate that with dietary iodine supplementation, there is a change in disease pattern with

increased prevalence of malignant (Harach, Escalante, & Day, 2002), toxic (Roti & Uberti, 2001) and inflammatory goitres (Harach et al., 1985). In populations that are iodine replete, like Kenya is, autoimmune thyroid disorders, Hashimoto's thyroiditis and Grave's disease should account for the vast majority of thyroid dysfunction (Weetman & McGregor, 1994). Furthermore, iodine deficiency is a known risk factor for follicular carcinoma while iodine sufficiency is associated with papillary thyroid carcinoma (Wartofsky, 2010). This would make the findings in this study unique and outlying. Accuracy of histological and FNAC examinations would be called into question; a fact illustrated by the finding of a low FNAC sensitivity of 43.6%, specificity of 96.4%, positive predictive value of 89.1% and a negative predictive value of 77.9% in the current study. This same question was raised by Watters et al (Watters & Wall, 2007) and Ogbera et al (Smyth, 2014). Thus, decisions based on FNAC concerning extent of resection would place the patient at an unnecessarily higher risk for postoperative complications. The low rate of malignancy in this study could also be explained by the possibility that patients with malignant goitre diagnoses were presenting at clinically advanced stages where surgical intervention was ill advised.

Globally, FNAC is the standard of care for nodules meeting size and ultrasonography characteristics as agreed by consensus (Chen et al., 2014). The overall FNAC accuracy for cytological diagnosis approaches 95% (Gharib & Goellner, 2003). Broken into its various components, this translates to a sensitivity 65–98%, specificity of 72–100%, positive predictive value of 50–96%, false negative rate of 1–11% and a false positive rate 0–7%. Trucut biopsy may be indicated where FNAC fails to provide sufficient sampling in lesions with fibrosis, rapid growth, invasion or pain that suggests anaplastic thyroid carcinoma or lymphoma. However, Trucut biopsy is associated with higher rates of hematoma, pain and

damage to the trachea and recurrent laryngeal nerve. Other ways of improving FNAC accuracy include the use of ultrasound guidance during sampling and molecular markers. Auxiliary imaging tests like CT scan, FDG–PET scan and MRI scans have been also found to play an important complimentary role.

It has been suggested that a multivariate approach that combines clinical, sonographic, cytological and molecular assessments is likely to be most successful in diagnosing benign and malignant thyroid pathology. (OKAMOTO et al., 1994).

5.3 Clinical observations

All patients received preoperative prophylactic antibiotics. This was despite knowledge of international guidelines that didn't routinely recommend systemic antibiotic prophylaxis (Nurses, 2002). This was justified by routine passive drain placement (94.6%) and prolonged hospital stay – 3.12±1.565 days in this study. Both of these factors were presumed to increase the risk of postoperative infection. Other studies in the country don't report antibiotic use. A Nigerian study did concur that use of antibiotics did not affect rates of wound infection post thyroidectomy (Kpolugbo et al., 2013). Further, an Italian study by Avenia et al provided level I evidence that antibiotics did not change clinical outcomes in thyroidectomy patients whether or not drains were used (Avenia et al., 2009).

Differences in intraoperative technical conduct were evident amongst the various surgeon specialisations. The ENT surgeons favoured extracapsular dissections, laryngeal nerve and parathyroid gland visual identification. General surgeons on the other hand, favoured subtotal resections with intracapsular dissection. Most surgeries were bilateral and subtotal thyroidectomy was the commonest (28.4%). Total and near total thyroidectomies constituted

5.4% and 8.1% respectively. This study showed that the extent of resection was related to operating time ($p = 0.001$) and length of hospital stay ($p = 0.001$). Comparison with regional studies shows agreement with the current one. Areas where more extensive resections were practiced (Bakheit et al., 2008; Chalya et al., 2011; Mohamed et al., 2009) reported an associated longer postop stay and higher postoperative complication rate. Limited resections are however plagued by high recurrence rates estimated at 10 – 30% (Delbridge et al., 1999). These recurrences usually present with a time lag of 10 to 30 years (Delbridge et al., 1999; Khadra, Delbridge, Reeve, Poole, & Crummer, 1992) making follow-up difficult. The prospect of re-operation always portends still higher rates of complications. Furthermore, there have been reports of carcinoma being found in thyroidectomy specimens that had previously been labelled as benign. Wagana et al, while primarily looking at solitary thyroid nodules, did note that 11% of clinically multinodular goitres without dominant nodules contained carcinoma (Wagana et al., 2002). In the current study, out of 40 bilateral procedures done, there were only 4 total and 7 near total thyroidectomies. Thus, there is potential for the remaining 29 (72.5%) cases to present later with recurrent goitres. Malignant foci may be found in some of these recurrences that will warrant extensive re-operative surgery with its attendant risks.

From the clinical observations above, i.e. varied types of dissection, inconsistent identification of the recurrent laryngeal nerves and parathyroid glands, different extents of resections largely based on operating surgeon's intraoperative decision making, it is evident that MTRH lacks guidelines to streamline intraoperative conduct. Protocols have been shown to improve clinical outcomes in other studies (Chen et al., 2014; Nikiforov et al., 2009; L Rosato et al., 2012). Currently there are efforts by the Italian association of

endocrine units and the American and British thyroid associations to come up with protocols to guide all aspects of the perioperative care of patients with goitres.

5.4 Early Complications of thyroidectomy

The incidence of complications has been found to be a sensitive measure of the quality of thyroidectomies being performed (McHenry, 2002). Reported complications after thyroidectomy are rare but their consequences can often be life threatening (Idris et al., 2013). In the current study, the overall complication rate was 33.8% (n = 25). There were no mortalities. Relevant studies in the country and regionally quoted much lower overall complication rates: Wagana et al 4.1% (Hill et al., 2004); Chalya et al 7.9% (Chalya et al., 2011); Dakubo et al 6.1% (Dakubo et al., 2013); Abebe et al 14.6% (Abebe et al., 2007). Taken in isolation, this would make the morbidity rate in the current study the worst in the region. A possible explanation to this was that the current study included minor complications while the other studies largely omitted them. The definitions of the various complications were also not always clearly stated making comparison difficult. Most of these studies did quote mortality rates which ranged from 0.5% - 3.4%. The higher figures in these studies generally corresponded to higher occurrence of fatal airway obstructions. Availability of critical care support at MTRH probably served to mitigate against this complication. All the three patients who had airway obstructions in this study were stabilized at the intensive care unit after reoperation. Zambudio et al, found an overall complication rate of 21% (Antonio Ríos Zambudio et al., 2004). This rate compares more favourably with the one in the current study due to similarities in scope and definitions of the various complications.

Patients with complications were generally of the same age group as their counterparts without complications. Further analysis showed that they stayed longer in hospital and underwent more extensive resections that took a longer time to perform. A preoperative diagnosis of carcinoma would lead to extended resections which in turn led to higher complication rates. This was true even when the diagnosis was erroneous. Though multivariate analysis was not possible (low numbers), it would appear that the one truly independent risk factor for the development of complications in this study was the extent of resection. Participating surgeon wasn't a confounder.

Analysis of the complications by the extent of resection showed a statistically significant association between more extensive resections and the occurrence of laryngeal nerve palsy ($p = 0.030$) and hypocalcemia ($p = 0.002$). Of note is that although there were only 4 total thyroidectomies performed, they accounted for 9 out of 39 post-operative complications. Taken together with five near total thyroidectomies performed, these "extensive resections" accounted for 16 out of the total 39 postoperative complications. Singly, subtotal thyroidectomy carried the bulk of the complications – 11 out of 39, probably because it was also the commonest operation performed.

Goitre grade, retrosternal extension, presence of comorbidities and surgeon factors were not found to be risk factors for complications in this study. This was in contradiction to numerous studies which positively associate them with complications (McHenry, 2002; A. Schwartz, 2005; A. R. Zambudio et al., 2004). Surgeon factors have been especially well studied and were evident even in the days of Theodore Bilroth. It is known that surgeons who are well trained and perform frequent operations achieve better results. In particular, surgeon experience has been found to be a significant factor in the rate of

hypoparathyroidism (A. R. Shaha & Jaffe, 1998). Some have also observed that surgical residents in training can perform complex extensive resections, and with low complications, if supervised by an experienced surgeon (Martin et al., 1989; A. Shaha & Jaffe, 1988). The concession was that what was important was how well the thyroidectomy was done rather than who did it. A possible explanation to the findings in the current study is that majority (81.1%) of the thyroidectomies are done by experienced general surgeons. The contributions of the ENT surgeons and residents bias the statistical analysis due to their small numbers. Furthermore, the residents generally did less extensive resections compared to the general or ENT surgeons. Direct comparisons between the residents and other surgeon categories was therefore not feasible.

In the current study, despite most patients with postoperative complications presenting with large palpable goitres, goitre grade did not show a significant association with the complications. Contrasted to this, MC Henry et al showed an increase in hypoparathyroidism rate with goitres >100g size and intrathoracic location (McHenry, 2002). Zambudio et al, in a 2004 study, found goitre grade and hyperthyroidism to be independent factors affecting complication rates (A. R. Zambudio et al., 2004).

Out of the 6 (8.1%) patients with retrosternal goitres, 4 had complications .i.e. 2 hypoparathyroidism and 2 seroma. All were grade III goitres and all patients had compressive symptoms which formed the indications for surgery. None of them were primarily intrathoracic and therefore all the operations were successfully done from a cervical approach. Literature agrees that the cervical approach is adequate in 94 – 98% of retrosternal goitres (Abboud, Sleilaty, Mallak, Abou Zeid, & Tabchy, 2010). It further concedes that partial or total sternotomy is only needed rarely 2 – 5% (White, Doherty, &

Gauger, 2008). These surgeries took longer to perform (140±85.24 minutes) and postoperative stay was prolonged (4.5±1.73 days). The 8.1% rate of occurrence was in agreement with other studies which gave a range of 2 – 19% (Rugiu & Piemonte, 2009). Studies have shown postoperative morbidity to be higher in patients with retrosternal goitres with increased risk of bleeding, hypoparathyroidism, recurrent laryngeal nerve injury and airway obstruction secondary to tracheomalacia (Abboud et al., 2010; Bakheit et al., 2008; Sancho et al., 2006). One reason for lack of statistical association between retrosternal goitres and complication occurrence in this study is probably low patient numbers. Additionally, it could be due to the varied definitions as to what constitutes a retrosternal extension (Abboud et al., 2010).

Hypoparathyroidism/hypocalcemia

The rate of hypoparathyroidism in this study was 12.2% (n = 9). Associated risk factors were extent of resection, FNAC diagnosis of carcinoma and type of dissection. Local studies largely fail to report this complication (Abebe et al., 2007; Chalya et al., 2011; Hill et al., 2004; Idris et al.; Mohamed et al., 2009; Wagana et al., 2002). Dakubo et al, in Ghana gave a rate of 1.9% (Dakubo et al., 2013) while Chalya et al, Tanzania gave 0.6% (Chalya et al., 2011). Chalya's study however did not use a biochemical definition for hypocalcemia. Dakubo did not state his definition. In her 2014 unpublished dissertation entitled "Incidence of Post thyroidectomy hypocalcemia in Kenyatta National Hospital" Peace Muige found an incidence of 68% (Peace, 2014). She used a purely biochemical definition of hypocalcemia and included patients who were hypocalcemic preoperatively. None of her patients were symptomatic. International studies quote a range of 0.33 – 65% (Mehanna et al., 2010). Associated risk factors in these studies include age, extent of resection, hyperthyroidism,

goitre grade, retrosternal extension and compressive symptoms (Acun et al., 2004; Bures et al., 2014; Delbridge et al., 1999; A. R. Zambudio et al., 2004). The wide range is attributed to the lack of a precise definition. Calcium levels in different studies are determined by different assays, at different perioperative times and using different definitions of normal values (Jessie & Harrison, 2010). In the current study, hypocalcemia was defined as total calcium level of < 1.875mmol/L and the presence of symptoms. All the patients who were symptomatic met this criteria. This was in line with studies elsewhere (Rios, Rodriguez, Balsalobre, Tebar, & Parrilla, 2010; A. R. Zambudio et al., 2004). The presence of a positive Chvostek test, trousseaus sign and peri-oral and limb paraesthesia was heavily relied on as a screening measure due to cost constraints. Support for this was additionally found in a study that showed that only one third of patients who developed biochemical hypocalcemia required treatment (Jessie & Harrison, 2010).

Only 20.3% (n = 15) of patients had their parathyroid glands visualised intraoperatively. One parathyroid was auto transplanted. There is disagreement in the literature about the usefulness of visualising the glands (Thomusch et al., 2000). To reduce hypoparathyroidism, routine auto-transplantation has been suggested. While some studies found one parathyroid to be sufficient (Dener, 2002), others believe that three glands are needed (Pattou et al., 1998). Still, others contend that in addition to gland auto-transplantation, routine identification, preservation of their blood supply and the use of near total thyroidectomy when the glands are at risk is what's needed to reduce rates to between 1 – 4% (A. Schwartz, 2005).

In the current study, 7 out of the 9 patients with postoperative hypocalcemia had extracapsular dissections done. These dissections, as alluded to by Schwartz et al (A.

Schwartz, 2005), typically enable definitive identification of the parathyroid glands and their subsequent preservation or transplantation. In this study, despite use of the technique, only one third of patients with hypocalcemia had their parathyroid glands visualised. Subsequently, none of the glands were auto-transplanted. All these operations were carried out by the general surgeons. Studies have shown that although initially associated with higher rates of transient hypocalcemia, parathyroid gland auto-transplantation eventually leads to reduced rates of permanent hypocalcemia (Pattou et al., 1998). Interestingly, further analysis of the current study shows that although the ENT surgeons extensively used an extracapsular dissection technique, none of the 10 thyroidectomies they performed were associated with postoperative hypocalcemia. They routinely identified and preserved the parathyroid glands (9 times out of 10 thyroidectomies) and were the only ones to carry out a parathyroid gland auto-transplantation.

In retrospect, the extracapsular dissection without parathyroid gland identification by the general surgeons could have inadvertently devitalised the glands by disrupting their precarious blood supply. In summary, parathyroid gland identification and preservation is a practice that should be widely adopted especially when carrying out extensive gland resections.

Recurrent laryngeal nerve injury

Thyroidectomy accounts for 35.7% of all surgical causes of recurrent laryngeal nerve injury and 3.7% of all causes (Idris et al.). Injury to this nerve is the cause of 2 -3% of all medico legal claims (Ready & Barnes, 1994). Together with hypoparathyroidism, their effect on the quality of life can be profound.

The rate of recurrent laryngeal nerve palsy in this study was 5.4% (n = 4). That of the external branch of the superior laryngeal nerve was 1.4% (n = 1). The extent of resection and FNAC diagnosis of carcinoma were the only independent risk factors associated with its occurrence. Other studies reveal that in addition to extent of resection, goitre grade, retrosternal location, surgeon factors and presence of compressive symptoms increase risk (Du et al., 2012; A. R. Zambudio et al., 2004). Surgeon factors were explored by Lamade and colleagues. They found that recurrent laryngeal nerve injury rates can increase two fold in newly qualified surgeons compared to established ones and even to surgical trainees under supervision (Lamade, Renz, Willeke, Klar, & Herfarth, 1999). They emphasized the need for general surgery training programmes to provide adequate experience in thyroid surgery. The current study stratified complications between general, ENT and trainee surgeons but found no statistical significance. However, it was noted that the ENT surgeons did extracapsular dissections and regularly visualised the recurrent laryngeal nerves and the parathyroid glands. This may explain why they had a 20% complication rate compared to the 37% in the general surgeons.

Local studies quote rates of palsy that are in agreement with the current one. Wagana et al practised regular visualisation of the recurrent nerves. His rate of palsy was 1.4% (Hill et al., 2004). In his unpublished dissertation, "Post thyroidectomy recurrent laryngeal nerve paralysis as seen at Kenyatta National Hospital, Nairobi-Kenya," Wahome got a rate of 8.8% (Wahome, 2007). Age, sex, extent of resection and experience of the surgeon were found to be not significant. He emphasized identification of the RLN as being pertinent to its preservation. Operations for recurrence and malignancy were found to increase risk. Wahome further noted that postoperative hoarseness tended to recover in six weeks. Most

patients with nerve palsy did present with hoarseness but a confirmatory laryngoscopy was necessary. These findings were echoed elsewhere (Lodovico Rosato, Carlevato, De Toma, & Avenia, 2005). Others state that more than a third of patients with unilateral RLN injury were asymptomatic. Voice changes could therefore not be relied upon as predictors of vocal cord function. The sensitivity of voice assessment used alone varied from 33% to 68%. Specificity was 75% and its positive predictive value was 38% (Farrag, Samlan, Lin, & Tufano, 2006; G. W. Randolph & Kamani, 2006).

In the current study, RLN were visualised in 25 (33.8%) of the patients. Unlike Wahome's study, there was no statistical association of significance between visualisation and the rate of RLN injury. However, a closer look at the patients who had visualisation of their RLN showed that 12% (n=3) went on to get a palsy of the nerve. In contrast, only 4.1% (n=2) of the 49 patients without RLN visualisation had a nerve palsy. These results may indicate a trend towards injury of the nerve concurrent with its identification. Other investigators have noted the same but argue that identification of the nerve is the only means of preventing its permanent injury. Recurrent laryngeal nerve palsies that occur in the setting of clear intraoperative identification and preservation tend to be transient neuropraxias (Idris et al., 2013).

Internationally, the incidence of RLN injury varies from <1% to 20%.The range difference reflects differences in: type of disease (benign or malignant); type of resection (1st time or recurrent goitre); extent of resection; surgical technique (identification of RLN or not) and surgeon experience (Barczyński, Konturek, & Cichoń, 2009).

Postoperative Bleeding.

Postoperative bleeding directly contributes to mortality in 0.01% of thyroidectomies. With reoperation, the rate rises to 0.6% (Promberger et al., 2012). The rate of postoperative bleeding as reported in literature stands at 0 – 5% **(Ozbas et al., 2005).** The rate of postoperative bleeding in this study was within this i.e. 2.7%. Both patients developed hematomas despite having drains in situ. There were no identifiable risk factors. The patients with this complication were comparable to those that did not.

Comparison with local studies shows a mixed picture. The range was from <1% to 33% (Abebe et al., 2007; Bakheit et al., 2008; Chalya et al., 2011; Dakubo et al., 2013; Hill et al., 2004; Mohamed et al., 2009). Chalya et al and El Bushra et al reported the higher rates and were noted to have more extensive thyroid resections their series (Chalya et al., 2011; Mohamed et al., 2009). In agreement with the current study, most hematomas and the consequent airway obstruction took <12 hrs to evolve. Other studies confirm this and emphasize the need for the patient to be observed for 24hrs in the least after bilateral procedures (Gerfo, 1998).

Meticulous attention to hemostasis is of paramount importance if one is to avoid this complication (Promberger et al., 2012).

Surgical site infections, seroma, flap edema, Airway obstruction

Surgical site infections account for a quarter of all nosocomial infections. They increase costs by necessitating re-hospitalisation, re-intervention, blood tests and medication.

Together with seromas and flap oedema, they alter clinical outcomes (G. Dionigi et al., 2008).

Site infection occurred in 3 (4.1%) patients. Age was a risk factor (p = 0.001) with all of them being >60yrs old. Diabetes was a comorbidity in one patient. All cases were preceded by seroma. All cases were evident by 7 days postoperative. These findings are in line with other studies (Avenia et al., 2009; G. Dionigi et al., 2008). Duration of hospital stay was not a risk factor in this study despite findings to the contrary by others (R. Dionigi et al., 2001; Green & Wenzel, 1977)

Seromas occurred at a rate of 8.1% (n = 6) and were associated with prolonged operations (p = 0.021). Flap edema occurred a rate of 6.8% (n = 5). There were no risk factors identifiable in this study.

Airway obstruction occurred in 3 (4.1%) patients in this study. These were secondary to tension hematoma and supraglottic edema in the face of a unilateral vocal cord palsy. Despite 95.9% of the goitres being grade II and III, and with 6 of them being retrosternal, there were no cases of tracheomalacia. None of the patients had a tracheostomy. In contrast to this, a 2001 Sudanese study by Bakhiet et al found a rate of 13%. All his patients needed a tracheostomy due to tracheomalacia. Also notable here was that he reported a retrosternal goitre extension rate of 46.3%.

6 Conclusions and Recommendations

6.1 Conclusions

1. Goitres in patients presenting for thyroidectomy at MTRH occur predominantly in females in their 5th and 6th decades of life. In comparison, regional studies show younger patients with lower female to male ratios.
2. There is an unexpectedly low rate of thyroid malignancy and inflammatory disorders in patients presenting for thyroidectomy at MTRH.
3. Early postoperative complications after thyroidectomy at MTRH are common compared to regional figures. Judged with this result, MTRH outcomes are not as good as global and regional outcomes.
4. Hypocalcemia is the commonest early postoperative complication after thyroidectomy at MTRH.
5. Patients who had an extracapsular type of dissection performed had higher rates of hypocalcemia compared to those with an intracapsular dissection.
6. Older age (over 60 years) was associated with higher rates of surgical site infections.
7. Extensive resection (total and near total thyroidectomy) was the most important factor associated with early postoperative complications at MTRH.
8. FNAC was found to be unreliable for making a preoperative diagnosis of thyroid cancer at MTRH.

6.2 Recommendations

1. **To Surgery Department MTRH**: Surgeons should have a high threshold for performing extensive resections (Total and Near Total thyroidectomy) in all goitres categories as these resections are associated with the highest rates of postoperative complications.
2. **To general surgeons, ENT surgeons and registrars**: Integrate information gotten from clinical and sonographic evaluations before FNAC. All FNAC procedures should be ultrasound guided.
3. **To MTRH, division of Surgery**: consider developing a perioperative protocol for thyroid surgery based on established global protocols. The protocol should include routine identification and auto-transplantation of the parathyroid glands in total and near total thyroidectomy.
4. **To MTRH, division of Surgery:** consider developing a policy on antibiotics in thyroidectomy based on established policies. The policy should include antibiotic cover for all elderly patients.
5. **To Pathology Department, MTRH**: Conduct formal audit on the efficacy of FNAC in MTRH to find out why its diagnostic index is lower than global figures.
6. **To Researchers**: Further long term studies and controlled clinical trials involving larger number of patients are needed to definitively delineate all factors contributing to occurrence of post-thyroidectomy complications at MTRH. The factors of interest would include: dissection type; role of recurrent laryngeal nerve and parathyroid gland visualisation; the incidence of thyroid neoplasm and its implications on the practice of thyroidectomy.

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7 Appendix I: CONSENT FORM

EARLY POSTOPERATIVE COMPLICATIONS OF THYOIDECTOMY AT THE MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA.

INVESTIGATOR – DR MULANDA GILBERT MUSASIA, P.O BOX 71, NGARA, NAIROBI, KENYA.

I _____of P.O Box_____

Tel_____

Hereby give informed consent to participate in this study in MTRH. The study has been explained to me clearly by Dr. MULANDA GILBERT MUSASIA.

I have understood that to participate in this study, I shall volunteer information regarding my medical condition, and undergo medical examination and I am aware that I can withdraw from this study any time without prejudice to my right of treatment at MTRH now or in the future. I have been assured that no injury shall be inflicted on me from my participation in this study. I have also been assured that all information shall be treated and managed in confidence.

Name of participant_____

Signature _____

Date _____

Name of witness_____

Signature _____

Date _____

APPENDIX II: QUESTIONNAIRE

SERIAL NUMBER:

Date Recruited into Study:

Name of Participant:

AGE:

SEX: Male ☐

Female ☐

Mobile Telephone Number:

Resident District:

Tribe: Kalenjin ☐ Kikuyu ☐ Luhya ☐ Kamba ☐ Mijikenda ☐

Maasai ☐ Luo ☐ Turkana ☐ Meru/Embu ☐ Somali ☐

Others: Specify……

Date of operation:

Duration of Hospital Stay after operation:

DIAGNOSIS: **Clinical:** Diffuse ☐ Nodular ☐

Toxic ☐ Non-toxic ☐

Solitary nodule ☐ Carcinoma ☐

Unilateral ☐ Bilateral ☐

Others:
Specify…….

Done☐ Not Done☐

Cytological (FNA): Colloid Goitre ☐

Thyroid Adenoma ☐

Carcinoma ☐

Others: Specify……..

Done☐ Not Done☐

Histological: Follicular Adenoma ☐ Follicular cyst ☐

Follicular Carcinoma ☐ Grave's Disease ☐

Hurthle cell carcinoma ☐

Papillary carcinoma ☐

Medullary Carcinoma ☐

Multinodular Goitre ☐

Lymphocytic infiltration: Yes☐ No☐

Others: Specify……

CORMOBIDITIES

Diabetes Mellitus Yes ☐ No☐

If yes, is disease controlled? Yes ☐ No ☐

Hypertension yes ☐ No ☐

If yes, is disease controlled? Yes ☐ No ☐

Bleeding Diathesis Yes ☐ No ☐

If yes, is disease controlled? Yes ☐ No ☐

Others: Specify……

PREMEDICATION

Anticoagulants yes ☐ No ☐

If yes, stopped before surgery? Yes ☐ No ☐

Antiplatelet agents yes ☐ No ☐

If yes, stopped before surgery? Yes ☐ No ☐

Prophylactic Antibiotics Yes ☐ No ☐

Other Medication: Specify……
…

LABORATORY INVESTIGATIONS

Full Hemogram: Platelets: Specify……..

WBC: Specify……..

Haemoglobin: Specify……..

Urea, electrolytes and Creatinine:Urea: Specify……..

Creatinine: Specify……..

Sodium: specify……..

Potassium: Specify……

Thyroid Function Tests (serum T^3, T^4, TSH)

Preoperative: TSH Levels: Specify……

Plasma Free T3: Specify…….

Plasma Free T4: Specify…….

Postoperative: TSH Levels: Specify……

Plasma Free T3: Specify…….

Plasma Free T4: Specify…….

Done☐ Not Done☐

INTRAOPERATIVE ASSESMENTS

Surgeon: Consultant ☐ Gen Surg☐ ENT☐

Registrar ☐ Number of years of practice in surgery: Specify……

Medical Officer ☐ Number of years of practice in surgery: Specify……..

Urgency of operation

Airway compression ☐ Cosmesis☐ Pain ☐

Oesophageal compression ☐

Type of Thyroidectomy:

Total ☐ Subtotal ☐ Near Total ☐ Lobectomy ☐

Partial lobectomy ☐ Excision of solitary nodule ☐

Isthmusectomy ☐ Dunhill Procedure☐ Hemithyroidectomy☐

Completion (for Recurrent goitre) ☐

Dissection

Capsular: Yes☐ No☐

Intra/Subcapsular: Yes☐ No☐

Goitre characteristics

Retrosternal Goitre Yes☐ No☐

Weight/Size of Goitre (WHO grade):……

Recurrent laryngeal nerve visualised: Yes ☐ No ☐

Parathyroid glands visualised: Yes ☐ No ☐

Duration of surgery in minutes: Specify……

OTHER ASSESMENTS

Vocal cords

Preoperative laryngoscopy **Hoarseness**: Yes☐ No☐

Done ☐ not done ☐

If Done: Normal cord motion ☐ Palsy of cord ☐

If Palsy present: Right ☐ Left☐ Bilateral ☐

Direct laryngoscopy at extubation **Hoarseness**: Yes☐ No☐

Done ☐ not done ☐

If Done: Normal cord motion ☐ Palsy of cord ☐

If Palsy present: Right ☐ Left ☐ Bilateral ☐

Postoperative Laryngoscopy at 2-6 wk. **Hoarseness**: Yes☐ No☐

Done ☐ not done ☐

If Done: Normal cord motion ☐ Palsy of cord ☐

If Palsy present: Right ☐ Left☐ Bilateral ☐

Postoperative wound site assessment

Primary postoperative bleeding:

First dressing changed in recovery room or within 12hrs because of bleeding: Yes☐ No☐

Volume of blood loss in the first 24hrs postop: Specify……

Blood pressure fall leading to hypotension Yes☐ No☐

Blood transfusion done: Yes☐ No☐

Patient Re-explored in theatre due to bleeding: Yes☐ No☐

If Yes, duration from surgery to re-exploration in hours:…….

Haematoma Formation:

Anterior midline swelling Yes☐ No☐

Airway compromise Yes ☐ No ☐

Surgical evacuation done: Yes ☐ No ☐

Presence of a seroma Yes ☐ No ☐

If Yes, Intervention done: Serial percutaneous needle aspiration ☐

Expectant management ☐

Surgical Site infection Yes ☐ No ☐

If Yes: Superficial ☐ Deep ☐

Interventions: Continued occlusive dressing ☐

Wound laid open for drainage ☐

Debridement/necrotomies done ☐

Flap oedema: Yes ☐ No ☐

Assessment of postoperative hypocalcemic state

Clinical signs

Chvostek's positive Yes☐ No☐

Trousseau's positive Yes☐ No☐

Clinical Symptoms

Perioral tingling/finger numbness: Yes☐ No☐

Others:
Specify……
……

Serum Calcium Levels: Specify…….

Done☐ Not Done☐

N/b: Serum calcium levels and postoperative thyroid function tests are checked at six weeks postop.

Use of drains

Yes☐ No☐

Appendix III: IREC approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2012/175
Approval Number: 000876

30th August, 2012

Dr. Mulanda Gilbert Musasia,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Mulanda,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee have reviewed your research proposal titled:

"Early Postoperative Complications of Thyoidectomy at the Moi Teaching and Referral Hospital, Eldoret, Kenya."

Your proposal has been granted a Formal Approval Number: **FAN: IREC 000876** on 30th August, 2012. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 29th August, 2013. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Yours Sincerely,

APPROVED
30 AUG 2012

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc:	Director	-	MTRH
	Principal	-	CHS
	Dean	-	SOM
	Dean	-	SPH
	Dean	-	SON
	Dean	-	SOD

Appendix IV: MTRH Approval

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

30th August, 2012

Dr. Mulanda Gilbert Musasia,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"Early Postoperative Complications of Thyoidectomy at the Moi Teaching and Referral Hospital, Eldoret, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. J. KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM