

"PRESENTATION AND SURGICAL
MANAGEMENT OF HYPERTHYROIDISM
IN KENYATTA NATIONAL HOSPITAL"

INVESTIGATOR:

DR. KENNETH K. SIGILAI (MBChB)(Nairobi)

*A dissertation submitted as part fulfilment for the degree of Master of Medicine
(Surgery) of the University of Nairobi*

**MEDICAL LIBRARY
UNIVERSITY OF NAIROBI**

SUPERVISOR

PROFESSOR JOHN A. ADWOK

Associate Professor

Department of Surgery

University of NAIROBI Library



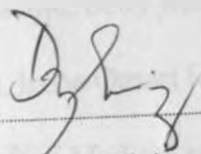
0324915 8

University of Nairobi

DECLARATION

I certify that this dissertation is my original work and it has not been presented for a degree programme in any other university

Signed



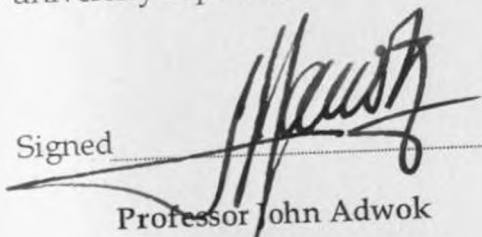
Dr. K.K. Sigilai

Date

27.1.2008

This dissertation has been submitted for examination with my approval as a university supervisor

Signed



Professor John Adwok

Date

27.1.2008

ACKNOWLEDGEMENT

I would like to thank the following persons who assisted me accomplish my project.

1. Professor John Adwok; for his supervision, guidance, criticism and support during the entire study period.
2. Mr. J. Njeru of clinical Epidemiology Unit for the statistical advice.
3. My sister, Betty Maina for use of her computer and editorial advice.
4. Mrs. Irene Omari for formatting and editing the manuscript.
5. Staff of Medical records department, KNH for retrieval of patient's files.
6. Kenyatta National Hospital Ethical and Research Committee for granting me permission to undertake this research in KNH.
7. My family; wife; Joyce, daughter; Memo and son; Kipngeno for putting up with my absence during the duration of my studies.

DEDICATION

I dedicate this work to my father, the late Mr. Paul A. Maina for the inspiration to aim for 'higher' goals in life and to my family: mother; Rosa, wife; Joyce, children; Memo and Kipngeno, for their patience and support.

TABLE OF CONTENTS

DECLARATION	II
ACKNOWLEDGEMENT.....	III
DEDICATION.....	IV
LIST OF FIGURES AND TABLES.....	VI
ABBREVIATIONS	VII
EXECUTIVE SUMMARY	VIII
INTRODUCTION.....	1
LITERATURE REVIEW	3
OBJECTIVE OF THE STUDY	24
RATIONALE OF THE STUDY	25
STUDY DESIGN	26
RESULTS.....	29
DISCUSSION.....	45
CONCLUSIONS.....	51
RECOMMENDATIONS.....	52
APPENDIX 1.....	53
APPENDIX 2.....	62

LIST OF FIGURES AND TABLES

	Page:
Figure 1: Age distribution of Toxic goitre	30
Figure 2: Geographical distribution of patients	31
Figure 3: Occurrence of Toxic Goitre	32
Figure 4: Complaints at presentation	33
Figure 5: Clinical Signs	34
Figure 6: Clinical classification of Toxic goitre	35
Figure 7: Final classification of various Toxic Goitres	37
Figure 8: Types of Thyroidectomy performed	41
Figure 9: Post-operative complications	42
Figure 10: Long-term outcome of surgery	43
Table 1: Results of Thyroid function tests	35
Table 2: Duration of Medical treatment	38
Table 3: Duration of pre-operative medical treatment	39

ABBREVIATIONS

AF:	Atrial Fibrillation
AFTNs:	Autonomously Functioning Thyroid Nodules
CCF:	Congestive Cardiac Failure
FNAC:	Fine Needle Aspiration Cytology
F-T3:	Free Triiodothyronine
F-T4:	Free Thyroxine
HTN:	Hypertension
KNH:	Kenyatta National Hospital
MNG:	Multinodular Goitre
RLN:	Recurrent Laryngeal Nerve
STNs:	Solitary Thyroid Nodules
T3:	Triiodothyronine
T4:	Thyroxine
TFTs:	Thyroid Function Tests
TRH:	Thyrotropin Releasing Hormone
TSH:	Thyroid Stimulating Hormone

EXECUTIVE SUMMARY

Hyperthyroidism is the second commonest endocrine disease seen in Kenyatta National Hospital (KNH), second only to diabetes mellitus. Every year about forty new patients with hyperthyroidism are recruited in the thyroid clinic while another fifty-seven undergo thyroidectomy for various forms of goitres, majority whom are hyperthyroid.

Though anecdotal evidence point to diffuse goitre as the main cause of hyperthyroidism, no survey has been done to classify the clinical presentation, surgical management and outcome of various hyperthyroid states as seen in KNH.

A ten-year retrospective study was designed to look into the presentation of hyperthyroidism as seen in KNH and subsequent surgical management. Outcome was assessed for the immediate post operative period and up to one-year post operatively.

The Main Findings Were:

The disease is more common in females with a male: female ratio of 1:4.2 and peak incidence at 37 years. Grave's disease affects a younger population with

average age of 31 years while Toxic Multinodular Goitre occurs in people 10 years older.

The commonest presenting symptoms were a neck swelling, heat intolerance and palpitations while the main clinical signs were goitre, tachycardia and exophthalmos.

During the study period only 39% of the patients were managed surgically though these had a better long-term outcome with 70% remaining Euthyroid one year after surgery as compared to only 20% of those managed medically.

Conclusion

Surgical management of toxic goitre is effective with 70% patients remaining euthyroid one year after surgery. Surgery should be adopted for most patients, especially those with poor drug compliance or cannot afford long-term drug therapy. The complications of surgery can be minimised with proper training of all surgeons.

INTRODUCTION

Definitions:

Hyperthyroidism: Sustained thyroid hyper function associated with a sustained increase in thyroid hormones biosynthesis and release from the thyroid gland.

Thyrotoxicosis: The clinical syndrome that results when the circulating concentrations of free thyroxine and triiodothyronine are increased.¹

Among the causes of spontaneously occurring hyperthyroidism, Grave's disease is undoubtedly the most common. Its frequency of causing thyrotoxicosis ranges from 60% to 90% in different parts of the world. Toxic multinodular goitre accounts for between 20% to 30% of the cases and solitary thyroid nodules causes thyrotoxicosis in about 5% to 10% of the cases.² Less common causes of thyrotoxicosis include iodine-induced hyperthyroidism, human chorionic gonadotropin associated thyrotoxicosis and pituitary resistance to thyroid hormone regulation, in which free thyroxin is elevated in clinically euthyroid or hypothyroid patients but thyroid stimulating hormone is normal to increased. Nonhyperthyroid thyrotoxic states are associated with low radioactive iodine uptake ratios as seen in the three types of sub acute

thyroiditis, ectopic hormone production or exogenous ingestion of thyroid hormone. Management of thyrotoxicosis requires lowering of thyroid levels to maintain a euthyroid state. Antithyroid drugs, radioactive iodine and surgery are the principal forms of treatment. Prolonged follow up is necessary in all cases. ³

LITERATURE REVIEW

Historical Background

The history of the thyroid gland has been admirably summarised by Rollenstone ⁴ and Thompson ⁵ and carefully detailed for Graves' disease by Sattler.⁶

Visible neck swellings have been reported for the past twenty-five centuries while their nature, appearance, causes and management have been subject of countless reports. The fullness or swelling of the neck caused by thyroid enlargement was referred to by the Greeks, including Gallen as '*Bronchocoele*' (hernia or swelling of the wind pipe) and this term was used as late as 1800 AD.⁵ The later term introduced by Philny and Juvenal, '*tumid gutter*' (*swollen throat*), eventually became French *goitre*, and later the English *goitre* (in America *goiter*).⁷

Gallen in his '*De Voce*'⁷ described some secreting gland adjacent to the part of the larynx the anatomist called the thyroid cartilage because of the shield shape of this structure. Eustachian termed the adjacent glands the '*laryngeal gland*'.⁸ They remained the laryngeal glands until Wharton in 1656 ⁵ named them the '*glandulae thyroidae*' (*thyroid glands*) because of their anatomical proximity to the thyroid cartilage and not because of their shape.

Thompson⁵ also points out that the thyroid was in fact a single gland and that 'Bronchocoele' (goitre) or 'fabricius' strummer (tumefaction) was a disease of the thyroid and that tumours occurred not only in the thyroid gland but also in 'bronchocaele' (goitre) as well. A Hard tumour mass was termed *schirrus* when there was no spread or ulceration, *cancer* when these developed.

The relationship between the thyroid gland and the various body functions was studied by experimental thyroidectomy as early as 1827⁹ and the concept of internal secretory function was formulated by King nine years later.¹⁰ The Reverdins and Kocher became aware of the similarities between myxaedema and the clinical picture that develops after successful removal of the thyroid.^{11, 12}

Hyperthyroidism was probably first described by Parry in 1825,¹³ when he recorded heart failure associated with swelling in the thyroid area. One of his five patients seen in 1786 had 'a remarkable extrusion of the globes from the sockets'. Parry attributed the neck swelling to a bronchocaele. In 1835 Graves collected three patients with marked palpitations and swelling of the thyroid; he recounted a fourth, related to him by a friend whose eyeballs were apparently 'enlarged' so that when he slept or tried to close her eyes the lids were incapable of closing and when she was awake her eyes showed the 'white

sclerotic' all around the cornea.¹⁴ Von Basedow in 1840 described the gourmet of eye changes and most other clinical features of the disease. He believed that the disease was an odd manifestation of tuberculosis.¹⁵

Graves' disease as labelled by Trousseau has become most favoured as an eponym because of Graves' acceptance of the thyroid swelling as the cause of the clinical disorder. The eponym Von Basedow's disease is used mainly in mainland European literature.

Recognising the role of thyroid gland in toxic goitre, Rehn performed in 1884 the first subtotal thyroidectomy.¹⁶ Magnus Levy was the first to describe the characteristic elevation of basal metabolic rate in the disorder.¹⁷

ANATOMY, PHYSIOLOGY AND PATHOLOGY OF HYPERTHYROIDISM

The thyroid gland develops as an endodermal thickening in the floor of the primordial pharynx about twenty-four days after fertilisation. This thickening soon forms a small out pouching - the thyroid diverticulum. As the tongue and embryo grow, the developing thyroid gland descends in the neck passing ventral to the hyoid bone and laryngeal cartilage to its definitive site in the neck.

At first, the thyroid diverticulum is hollow, but soon it becomes solid and divides into right and left lobes, which are connected by an isthmus of the thyroid gland, which lies anterior to the second and third tracheal rings. By seven weeks, the thyroid gland has assumed its definitive shape and has reached its final site in the neck. In fifty percent of the people, there is a pyramidal lobe, which represents a persistent part of the distal end of the thyroglossal duct. The gland weighs 15 to 25 grams in the normal adult. ¹⁸

The thyroid tissue is composed of follicles that consist of a simple epithelial sphere whose lumen contains colloid, a gelatinous substance. A loose connective tissue capsule that sends septae into the parenchyma covers the gland. The thyroid is an extremely well vascularized organ, with an extensive blood and lymphatic capillary network surrounding the follicles. This facilitates the passage of hormones into the blood capillaries. ¹⁹

The thyroid gland is innervated via the sympathetic and parasympathetic autonomic nervous system, which serves essentially a vasomotor function. The major regulator of the anatomic and functional state of the thyroid gland, however, is the *Thyroid Stimulating Hormone (TSH, Thyrotropin)*, which is secreted by anterior pituitary gland. ¹⁹

Another type of cell, the *Parafollicular cells (C-cells)* are found as part of the follicular epithelium or as isolated clusters between thyroid follicles. The c-cells are neuroendocrine in origin, arising from Ultimobranchial bodies, which develop from the ventral portion of the fourth pharyngeal pouch. These cells are responsible for the synthesis and secretion of *calcitonin*, a hormone whose main effect is to lower blood calcium levels by inhibiting bone resorption. ¹⁹

When the gland is inactive, the colloid is abundant, the follicles are large and the cells lining them flat. When the gland is active, the follicles are small the cells are cuboid or columnar and the edge of the colloid scalloped, forming many small 'resorption lacunae'. ²⁰

THYROID HORMONES SYNTHESIS, SECRETION AND REGULATION

Thyroid cells collect and transport iodine, synthesise thyroglobulin and secrete it into the colloid and remove the thyroglobulin and secrete them into the circulation. Control of thyroid hormones synthesis and release is mainly under the hypothalamo-hypophyseal-thyroid regulatory system

Thyroid hormones secretion and release is regulated by thyrotropin (TSH), which in itself is under the influence of thyrotropin releasing hormone (TRH). The effect of T3 and T4 on peripheral tissues and their plasma levels regulates the secretion of TRH and TSH by a negative feedback mechanism. ²⁰

➤ Physiologic Effects of Thyroid Hormones

Thyroid hormones have two main physiologic effects:

1. They increase protein synthesis in virtually every body tissue thereby influencing growth and development.
2. They increase oxygen consumption by increasing the activity of the Na^+/K^+ ATPase primarily in the tissues responsible for basal oxygen consumption (i.e. liver, heart, and skeletal muscles)

Mechanism of action:

The hormone binds to thyroid receptor in the nuclei; the hormone-receptor complex then binds to DNA and increases (or in some cases decreases) the expression of a variety of different genes that code for enzymes, which regulate cells functions. ²⁰

➤ Pathophysiology of Hyperthyroidism

Hyperthyroidism occurs when there is a sustained thyroid hyper function associated with a sustained increase in thyroid hormone biosynthesis and release from the thyroid gland.

Patients present with weight loss despite increased appetite, weakness, hyperkinesia, nervousness, and irritability and emotion lability. There is heat intolerance, excessive sweating, a fine tremor, tachycardia, and an increased

cardiac output; palpitation; and breathlessness may occur. In older patients atrial fibrillation and cardiac failure may be the presenting feature.

Most of the signs and symptoms of hyperthyroidism are due to the increased sensitivity to circulating adrenaline because of enhanced B-adrenergic responsiveness, an example of hormone/ hormone interaction. ³

The most common cause of hyperthyroidism is Graves' disease accounting for up to 80% of cases. Toxic Multinodular Goitre is implicated in about 10% and Toxic Solitary Nodule (Adenoma) in 5-10%. Other cases are rarer: Hashimoto Thyroiditis, TSH secreting Pituitary Adenoma, ingestion of thyroid hormone and Jod-Basedow phenomenon.³

TYPE OF THYROTOXICOSIS

PATHOGENIC MECHANISM

Thyrotoxicosis associated with hyperthyroidism

- **State of excess TSH**

Tumour

Thyrotroph adenoma

Non-tumour

Thyrotroph resistance to thyroxin

- **Abnormal thyroid stimulation**

Graves' disease

TSH receptor antibody

Trophoblastic tumour

Chorionic Gonadotropin

- **Intrinsic thyroid autonomy**

Toxic Adenoma

Benign tumour

Toxic Multinodular Goitre

Foci of functional autonomy

Thyroid cancer

Foci of functional autonomy

Thyrotoxicosis not associated with hyperthyroidism

- **Inflammatory disease**

Silent thyroiditis

Release of preformed hormones

Sub acute thyroiditis

Release of preformed hormones

- **Extra thyroidal source of hormone**

Exogenous hormone use

Hormone in medicine or food

Ectopic thyroid tissue

Dermoid tumour (Stoma ovarii)

DIAGNOSIS OF THYROTOXICOSIS

✍ Clinical Diagnosis

The symptoms and signs of thyrotoxicosis often create a pathognomonic clinical picture. Diagnostic indices based on these clinical features accurately identify most patients with overt thyrotoxicosis though it correlates poorly with its biochemical severity. There is considerable variability among patients in specific clinical features and their severity. Specific signs are diagnostic of some conditions for example; exophthalmos, thyroid achropatchy, and localized myxaedema are present in Graves' disease while sub acute (de Quervain's) thyroiditis has a characteristic presentation with pain, fever and malaise.^{27, 28}

✍ Laboratory Diagnosis

Laboratory confirmation of thyrotoxicosis has traditionally been based on detection of elevated total and free concentrations of thyroxine (T4) and triiodothyronine (T3) in serum (or plasma). In most cases, the total and free concentrations of both are elevated, but isolated increases in T4 or T3 also occur. TSH assay in thyrotoxicosis is also useful in diagnosis. In most cases, TSH is decreased.²⁹

TYPE OF THYROTOXICOSIS

PATHOGENIC MECHANISM

Thyrotoxicosis associated with hyperthyroidism

- **State of excess TSH**

Tumour

Thyrotroph adenoma

Non-tumour

Thyrotroph resistance to thyroxin

- **Abnormal thyroid stimulation**

Graves' disease

TSH receptor antibody

Trophoblastic tumour

Chorionic Gonadotropin

- **Intrinsic thyroid autonomy**

Toxic Adenoma

Benign tumour

Toxic Multinodular Goitre

Foci of functional autonomy

Thyroid cancer

Foci of functional autonomy

Thyrotoxicosis not associated with hyperthyroidism

- **Inflammatory disease**

Silent thyroiditis

Release of preformed hormones

Sub acute thyroiditis

Release of preformed hormones

- **Extra thyroidal source of hormone**

Exogenous hormone use

Hormone in medicine or food

Ectopic thyroid tissue

Dermoid tumour (Stoma ovarii)

⚡ Graves' Disease

Graves' disease is a form of hyperthyroidism associated with a diffusely hyperplastic goitre resulting from an antibody directed against the thyroid stimulating hormone (TSH) receptor which act as an agonist for TSH. The incidence of Graves' disease is reported to be 0.02-0.4% of the population in USA and about 1% in Northern England.²¹

Graves disease appears most commonly between the ages 20-50 years. Presenting features are; thyrotoxicosis, enlarged thyroid gland, ophthalmopathy, localised myxaedema and thyroid acropachy.

Course: Variable. Some undergo unrelenting course; others show cyclical remission and recurrence.

Diagnosis: Increased T3, T4, Decreased TSH, with diffuse goitre with or without ophthalmopathy. Others: 24 hrs Iodine¹³¹ uptake test or radioisotope scan.

⚡ Toxic Multinodular Goitre (Plummer's Disease)

Thyrotoxicosis in multinodular goitre occurs when the number of newly generated follicles with at least some degree of autonomous iodine metabolism

becomes large enough so that overall hormone production exceeds the needs of the individual.

Because the generation of new follicles is a slow process, development of thyrotoxicosis in multinodular goitre is insidious over a period of several years.

It predominantly affects older people with long standing goitres.^{22, 23}

✦ Solitary Thyroid Nodules (Autonomously Functioning Thyroid Nodules) (Aftns)

These discrete thyroid nodules function independently of the normal pituitary-thyroid negative-feedback control mechanism. AFTNs may be solitary in otherwise normal glands or they may appear as single or multiple nodules in multinodular goitre.

AFTNs are classified as:

Adenomas: Benign encapsulated tumour showing evidence of follicular cells differentiation. These are usually solitary and have a well-defined fibrous capsule.

Adenomatous lesion: Used to describe lesions that are circumscribed but not encapsulated.²⁴

DIAGNOSIS OF THYROTOXICOSIS

✍ Clinical Diagnosis

The symptoms and signs of thyrotoxicosis often create a pathognomonic clinical picture. Diagnostic indices based on these clinical features accurately identify most patients with overt thyrotoxicosis though it correlates poorly with its biochemical severity. There is considerable variability among patients in specific clinical features and their severity. Specific signs are diagnostic of some conditions for example; exophthalmos, thyroid achropachy, and localized myxaedema are present in Graves' disease while sub acute (de Quervain's) thyroiditis has a characteristic presentation with pain, fever and malaise.^{27, 28}

✍ Laboratory Diagnosis

Laboratory confirmation of thyrotoxicosis has traditionally been based on detection of elevated total and free concentrations of thyroxine (T4) and triiodothyronine (T3) in serum (or plasma). In most cases, the total and free concentrations of both are elevated, but isolated increases in T4 or T3 also occur. TSH assay in thyrotoxicosis is also useful in diagnosis. In most cases, TSH is decreased.²⁹

◀ Differential Diagnosis

The various forms of thyrotoxicosis require differentiation for effective treatment. In many patients, the history and physical examination alone are sufficient. In other circumstances, additional laboratory or radionuclide studies are required to establish the cause and guide therapeutic decision-making.

Exuberant T3 production accompanies Graves' disease and many cases of toxic nodular goitre. (i.e., T3/T4 ratio greater than 20). T4-predominant thyrotoxicosis (i.e., T3/T4 less than 15) suggests that thyroiditis (sub acute or silent), iodine-induced thyrotoxicosis, or exogenous l-thyroxin may be involved. Radionuclide studies are needed in differential diagnosis in only a minority of patients. Forms of hyperthyroidism caused by excessive glandular hormonogenesis typically are accompanied by increased fractional radioisotope uptake in functional tissue, whereas glandular inflammation and suppression by extra thyroidal hormone production or ingestion are associated with low thyroidal radioisotope uptake. An elevated erythrocyte sedimentation rate is characteristic finding in sub acute thyroiditis, but not in silent thyroiditis.²⁹

TREATMENT OF THYROTOXICOSIS

The ideal treatment of thyrotoxicosis would be treatment of its cause. This is possible only in a few patients e.g. those with exogenous thyrotoxicosis or TSH-

secreting pituitary adenoma. However, patients with the common causes of thyrotoxicosis, i.e. Graves' disease, Autonomously Functioning Thyroid Nodules (AFTN) and Multinodular goitre, the fundamental causes are unknown. Therapy is therefore directed to destroying thyroid tissue, inhibiting thyroidal thyroxine and triiodothyronine synthesis and release and ameliorating the impact of the hormones on peripheral tissues, alone or in combinations. The main forms of treatments are antithyroid drugs, radioactive iodine and thyroidectomy.

The choice of treatment is yet to be unanimously agreed upon and varies intercontinentally. Antithyroid drugs are preferred in Europe and Japan³⁶ radioactive iodine is increasingly the treatment of choice in North America³⁸ while surgery is still the mainstay of treatment in Africa.³⁷ Costs of drugs, compliance and long follow-up periods are some of the reasons mentioned for this disparity.

TREATMENT OF GRAVES' DISEASE

ANTITHYROID DRUGS

Antithyroid drugs have been a mainstay of treatment of Graves' disease since their discovery in the mid-1940s'.³⁰ In a general way, these drugs inhibit the synthesis of thyroid hormones leading to a gradual reduction in serum thyroid hormones levels. After a while the dosage can be reduced or stopped all

together. These remissions do not occur in most patients and may not be lifelong even in those patients who achieve remissions. There are two classes of antithyroid drugs: the thionamides (e.g. propylthiouracil) and imidazoles (e.g. carbimazole or methimazole).

MECHANISM OF ACTION

The actions of antithyroid drugs are conveniently grouped into intrathyroidal and extra thyroidal effects.

Intrathyroidal activity ³¹

- Inhibition of iodine organification.
- Inhibition of iodotyrosine coupling.
- Possible alteration of the structure of thyroglobulin.
- Possible inhibition of thyroglobulin biosynthesis.

Extrathyroidal effects: ³²

- Inhibition of conversion of T4 to T3 (thiouracils and not imidazoles)
- Possible immunosuppressive effects (probably intrathyroidal as well).

ADMINISTRATION

Carbimazole is the antithyroid drug most commonly used. It is given in doses ranging from 15mg/day to 60mg/day.³³ Treatment is usually continued for two

years before remission occurs. There is low predictive indices of chance of remission though small size goitre, low initial biochemical levels and negative family history of Graves' disease in some cases is associated with long term (more than one year) remission. Suggestion of nearing remission is: reduction in the size of goitre; ability to control hyperthyroidism with small doses of drug and normalisation of the serum T4/T3 ratio³⁴ Continued thyroid enlargement, a continuing requirement for large doses of drugs and T3 predominant disease all portend a poor outcome on drug treatment.

Recurrence on antithyroid drug treatment is common. Recent studies show a recurrence rate of 60% at 5 years for a prolonged drug course (more than 2 years) and 91% recurrence for patients treated for less than one year³⁵

ADJUVANT THERAPY

β -Adrenergic antagonist agents:

β -adrenergic antagonist drugs have become an integral part of management of hyperthyroidism.³⁹ Many of the clinical manifestations of thyrotoxicosis mimic a hyperadrenergic state. Blockade of these receptors therefore provides patients with considerable relief from such symptoms as tremors, palpitations, anxiety and heat intolerance. Although propranolol is the drug that was originally used for thyrotoxicosis and is still used, a number of newer agents have a longer duration of action (atenolol, metoprolol, nadolol) or are more cardio selective

(atenolol, metoprolol). The standard starting dose of propranolol is in the range of 80-160mg/day⁴⁰

RADIOACTIVE IODINE

Since its introduction in the mid-1940s, radioactive iodine therapy has become the most widely used treatment for adults with hyperthyroidism in the United States of America⁴¹ Although other isotopes of iodine have been tried (e.g. I¹²⁵), they offer no clinical advantages and I¹³¹ has been and will continue to be the agent of choice.

Radioiodine is administered orally as a capsule or in water; it is rapidly and completely absorbed and quickly concentrated, oxidized and organified by the thyroid follicular cells. It emits both β and γ irradiation and destruction of follicular cells is due to the β particles.

Initially radioiodine produces an inflammatory response with transient mild tenderness and worsening thyroidal function. Over time atrophy and fibrosis, an associated chronic inflammatory response and ultimately results in thyroid gland failure. Histologically, cellular necrosis and inflammation are seen, as are bizarre nuclear changes reminiscent of malignancy⁴²

In general 50% to 75% of patients have normal thyroid functions and some shrinkage of goitre within 6-8 weeks after treatment. Overall approximately 75% are cured after a single dose, 10-20% require a second dose and a rare patient needs a third dose. Repeat doses is usually after six months has elapsed. ⁴³

COMPLICATIONS OF RADIOIODINE⁴⁴

Hypothyroidism: is considered an inevitable consequence of radioiodine treatment. It appears in 90% patients within first year of treatment and subsequently at rate of 2-3% every year for the remainder.

Thyroid and other tumours: There is concern of possible carcinogenicity with increase in thyroid cancer and cancer of the head and neck. However there is no tangible evidence so far.

Teratogenicity and chromosomal damage: this is possible. Radioiodine is absolutely contraindicated in pregnancy.

SURGERY

Sub-total thyroidectomy is the oldest form of therapy for hyperthyroidism. Although the Nobel Prize was awarded to Kocher in 1909 for his innovation in thyroid surgery, it was not until the introduction of iodine, and later

thianomides, as preparations for surgery that the mortality of surgery became acceptable. Although surgery has become an uncommon form of treatment for hyperthyroidism in the west, except in special circumstances, it is still a common mode in Kenya and the rest of sub-Saharan Africa.

The form of thyroidectomy done is sub-total thyroidectomy. In this procedure, the bulk of thyroid gland is removed, leaving a rim of a few grams of each lobe posteriorly⁴⁵

COMPLICATIONS OF THYROIDECTOMY

Mortality from sub-total thyroidectomy is close to zero. The common complications are recurrent laryngeal nerve injury and hypoparathyroidism, which occur in 1-2% of subtotal thyroidectomies.⁴⁶ Either of these can result in lifelong disability. Transient hypocalcaemia, post-op. bleeding, wound infection, keloid formation, unsightly scar occurs.

Hypothyroidism occurs in the first year of surgery in 6-10%⁴⁷ of patients with late onset of hypothyroidism developing in an additional 1-3% per year.⁴⁸ possibly reflecting the natural history of Graves' disease. The development of hypothyroidism is dependent on a number of factors, including the size of the remnant, the presence of antithyroid antibodies, perhaps reflecting autoimmune destruction of the remnant, and the duration of the follow-up⁴⁹

Recurrent hyperthyroidism develops in approximately 5% of the patients. This may develop many years after the surgery⁵⁰

Pre-operative preparation for surgery includes antithyroid drugs, iodides and β -adrenergic antagonist. The aim is to achieve a euthyroid state with a resting pulse rate less than 80 beats/min⁵¹

MULTINODULAR GOITRE⁵²

Because toxic multinodular goitre results from gradual multiplication of autonomous follicles, removal of excessive number of follicles by partial thyroidectomy or by radioiodine treatment is the treatment of choice. The younger the patient, the better is the patient's general health, and the larger the goitre, the more easily a surgical procedure is chosen. Radioiodine is optimal treatment in elderly patients with multiple health problems.

The aim of surgery of multinodular goitre is removal of all diseased micro- or macro nodular tissue. Goitre recurrence after surgery is rare though it cannot be entirely ruled out.

Hyperthyroidism is invariably reversible by treatment with antithyroid drugs. This therapy is not advisable, except in pre-op preparation, because it must be

given for a lifetime in most cases with increasing compliance problems in older patients.

SOLITARY THYROID NODULES (STNs)/AUTONOMOUSLY FUNCTIONING NODULES (AFTNS)

In a patient with AFTNs and is thyrotoxic, ablation of AFTN is indicated. Those with small asymptomatic nodules can be observed until symptoms develop. Patients with nodules greater than 3 cms with risk of developing thyrotoxicosis ablation of the nodules may be indicated. Two options of such ablation exist: surgery or radioiodine.

Surgery for STN is a simple and effective. Excision of the nodule itself with sparing of the remaining tissue is the procedure of choice. Since resection is less extensive, complications are fewer. Surgery offers the advantage of avoiding radiation to the rest of thyroid tissue. Recurrence of thyrotoxicosis after successful surgery of STNs is rare⁵³

Radioiodine treatment is as effective as surgery in treatment of STN. Because the nodules are relatively radio resistant, higher doses are required than for Graves' disease. Therefore, risk of cancer increase in a linear fashion. ⁵⁴ The development of hypothyroidism though is slower than for Graves' disease. ⁵⁵

Generally in treatment of STN, surgery is recommended for young patients and those with relatively large nodules (>3cm.). I¹³¹ is recommended for older patients and those with smaller nodules in whom radiation exposure of extranodular tissue does not represent a significant consideration.

OBJECTIVES OF THE STUDY

Broad Objective

To establish the presentation, surgical management and outcome of hyperthyroidism in Kenyatta National Hospital.

Specific objectives

1. To determine the prevalence of hyperthyroidism in KNH.
2. To classify the main causes of toxic goitres as seen in KNH.
3. To establish the modes of management of toxic goitre over the study period
4. To determine the outcomes of the goitres treated surgically.

RATIONALE OF THE STUDY

Thyrotoxicosis is still a common problem encountered in Kenyatta National Hospital (KNH). A thyroid clinic has been established to manage the patients presenting to KNH with the problem and every week approximately five new patients are recruited to the thyroid clinic while three to five patients undergo thyroidectomy in the same hospital. Anecdotal evidence indicates that the majority of these are due to toxic goitre. A study has not been done to determine the outcome of the patients managed surgically. My study aims at reviewing the surgical outcome of patients operated in the last ten years to justify this mode of treatment in our hospital.

Studies done elsewhere have found surgical treatment of toxic goitre to be a cost effective mode of treatment. Torre G. et al ²⁵ in their study of surgical outcome of surgery in toxic diffuse goitre in Italy found that stable euthyroid state is achievable and rates of complication small. Ahmed ME. et al ²⁶ has employed surgery as a cost effective method of managing toxic goitre in Khartoum teaching hospital. Therefore, surgery seems to be an effective means of managing thyrotoxicosis.

STUDY DESIGN

A descriptive retrospective study was conducted between January 1991 and December 2000. More than 300 new patients with thyrotoxicosis were seen during this period and over 100 of these managed surgically. The study population were all the patients seen at KNH during the study period with thyroid diseases. Patients with confirmed diagnosis of toxic goitre were eligible to be included in the study. Classification of patients as per the aetiology and mode of management was done for all the patients with toxic goitre. Outcome of surgical management was measured as per operative mortality, euthyroidism, recurrence, hypothyroidism and complications.

Patients and Methods

Study Site

The study was carried out at KNH, the country's main referral hospital and teaching hospital for the University of Nairobi.

Study Type

This is a hospital based retrospective study covering ten years from January 1991 to December 2000.

Study Plan

Retrieval of files from the hospital's records department of all patients

noted as having the disease of interest and the study of the patients' registers in Thyroid clinic, surgical wards and operating theatre. A proforma questionnaire was used to record all the required information.

Inclusion Criteria

All cases that were recorded as toxic goitre during the study period.

Exclusion Criteria

Case files that had incomplete or inadequate information for the purpose of analysis.

Case files that could not be traced.

Ethical Aspects

Application was made to and approval obtained from Kenyatta National Hospital Ethical and Research Committee to permit the study to be conducted in the institution. All patients' records were handled confidentially.

Data Collection

Information was collected as per:

Age, Sex, Geographical home, Presenting symptoms, Duration of illness, Clinical signs, Investigations done, Diagnosis, Management instituted,

Outcome of treatment, Outcome of surgery, immediate and in the long term.

Data Analysis

Data is presented using frequency tables, bar and pie charts and graphs.

Association between types of goitres, demographic data and outcome of surgery was investigated using Microsoft excel computer software.

Study Limitations

1. The sample size for my study was 323 patients but I managed to trace, analyse and include only 186 patients in the study. This could have been due to loss of files in medical records department or these were the actual patients seen in the hospital.
2. Lack of standardisation: Clinical assessment is subjective and prone to bias. Various laboratories use different units in reporting TFTs and there is no control or quality assurance.
3. Due to the cost of TFTs, not all patients could afford these mandatory investigations.
4. There is no published protocol for management of thyrotoxicosis in the hospital.

RESULTS

PATIENTS' PROFILE

Between 1991 and 2000, 356 patients with hyperthyroidism were seen and managed in Kenyatta National Hospital. I was able to trace and retrieve files for 218 patients. From this, only 186 satisfied inclusion criteria in this study. A further 24 patients were excluded from the study because of inadequate information in their files.

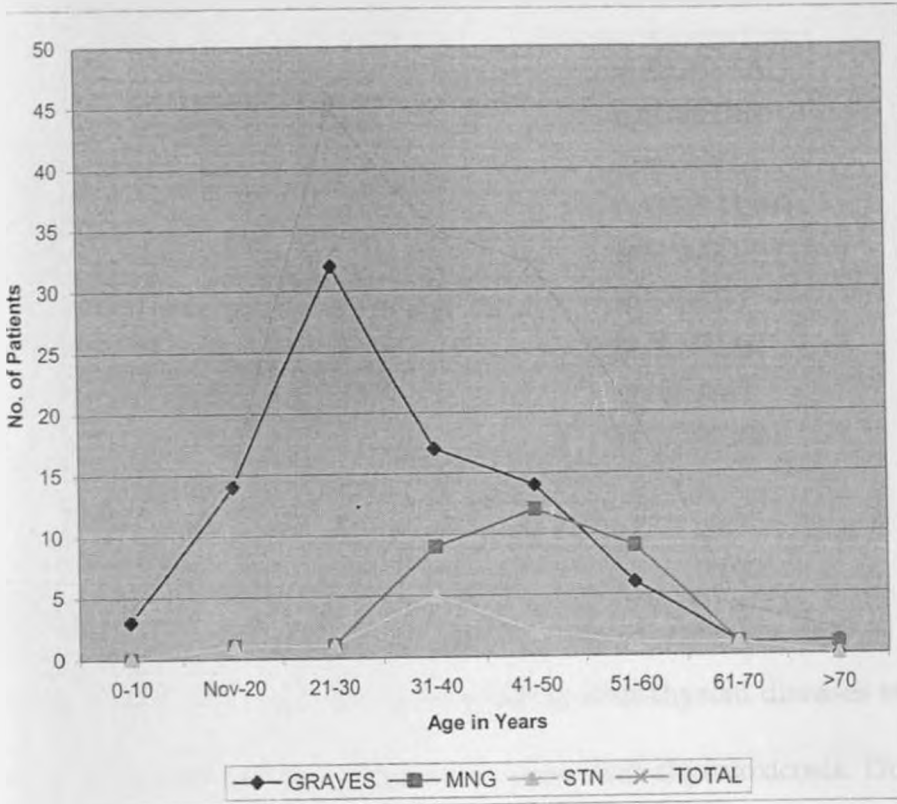
a. Sex

Of the 162 patients included in the study, 142 were females and 30 males. This gives a male to female ratio of 1:4.7.

b. Age:

The peak age group for thyrotoxicosis is 37 years. However the various thyrotoxic diseases had varied peak incidences. Grave's disease tends to affect a younger age group. Average age group for Grave's disease is 31 years; toxic multinodular goitre had a peak incidence at 41 years while solitary toxic nodules' averaged at 33 years. The youngest patient seen was 7 years old and the oldest was 78 year old.

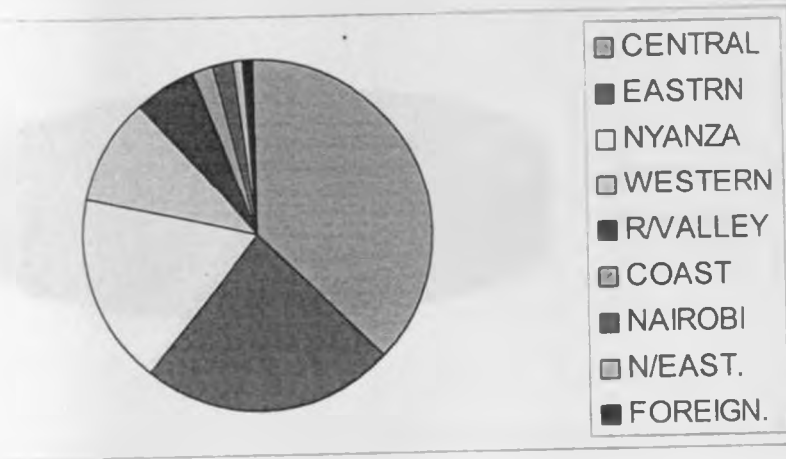
Figure 1: Age Distribution of Toxic Goitre.



c. Home Province

Majority of the patients seen in KNH came from central province. They constituted 38%. Eastern province came second with 24%. The others were as follows: Nyanza 18%, Western 10% and Rift Valley 6%. Coast and Nairobi each had 2% of the patients while North Eastern province and Foreigners constituted less than 1% respectively.

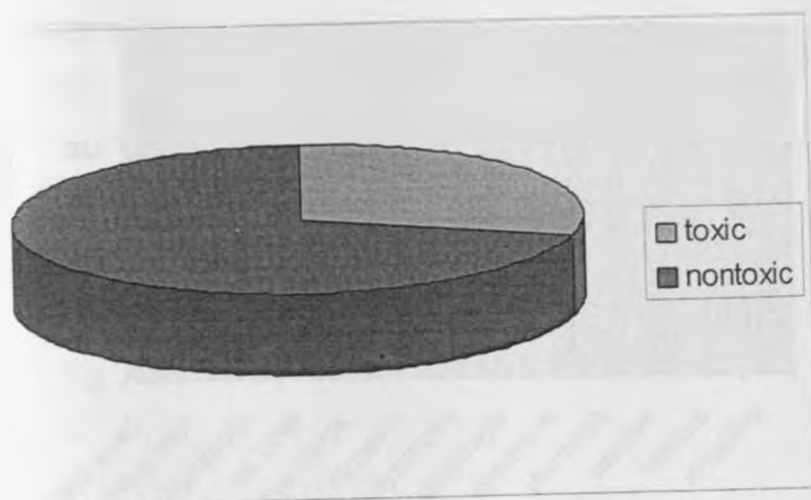
FIGURE 2: GEOGRAPHICAL DISTRIBUTION OF PATIENTS



PREVALENCE

Between the year 1991 and 2000, 1206 patients with thyroid diseases were seen in KNH. Three hundred and fifty-six of these had thyrotoxicosis. During the same period, 1,172,618 patients were seen in KNH. This gives prevalence of hyperthyroidism of 3 in 10,000 patients in KNH. The rate of toxic goitre during the same period was 29.5% of all goitre patients.

Figure 3: Occurrence of Toxic Goitre.

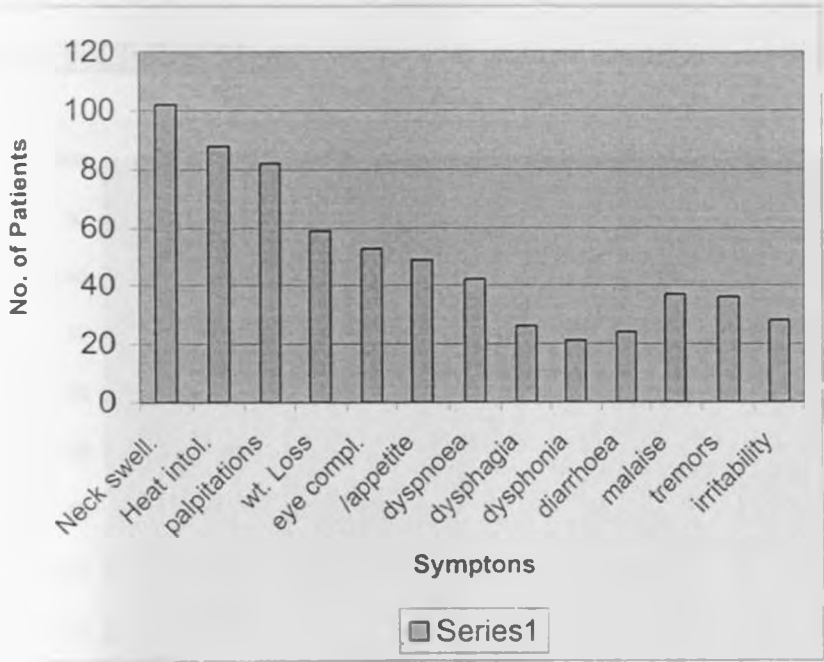


CLINICAL PRESENTATION

Symptoms

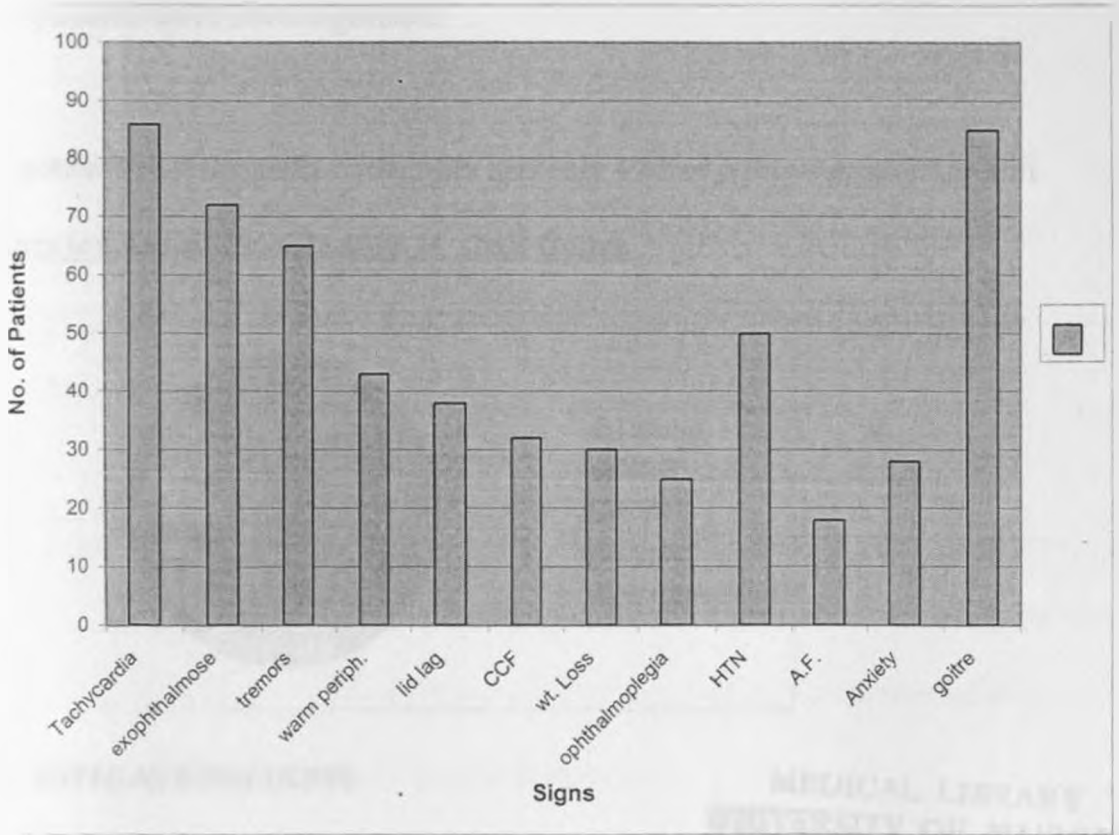
The commonest symptoms were: neck swelling occurring in 102(65%) patients, heat intolerance recorded in 88(56%) patients, palpitations in 82(52%) patients, weight loss in 59(38%), eye complaints in 53(34%) and increased appetite in 49(31%) patients. Other complaints were: behavioural change in 18%, fatigue in 24%, fine tremors in 22%, dyspnoea in 27%, dysphagia in 17% and dysphonia in 14% of the patients. Thirteen (8%) patients had a positive family history of hyperthyroidism.

Figure 4: Complaints at presentation



Signs:

Figure 5: Clinical Signs.

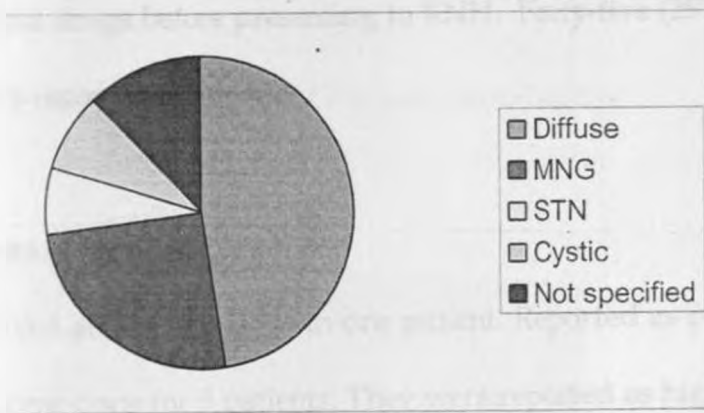


Tachycardia (55%), exophthalmos (40%), fine tremors (41%), systolic hypertension (32%) and moist /warm peripheries (28%) were the commonest presenting signs. Other signs were lid lag (24%); oedema and / or CCF (20%) weight loss (19%), anxiety (21%), ophthalmoplegia (16%) and atrial fibrillation (11%).

Goitre was present in 85% of hyperthyroid patients. Of these goitres, 48% were diffuse, 25% were multinodular, 7% solitary nodules and 8% cystic. Another 12% patients were not categorised.

All patients had the goitre in the neck and only 4% had a retrosternal extension.

Figure 6: Clinical Classification of Toxic Goitre.



INVESTIGATIONS DONE

Thyroid function tests

MEDICAL LIBRARY
UNIVERSITY OF NAIROBI

Table 1: Results of Thyroid Function Tests (TFTs)

	Normal	Low	High	Very High (>3x normal)
T4	22	-	72	18
T3	25	-	64	22
FreeT4	10	-	7	7
Free T3	6	-	9	6
TSH	26	79	-	-

Thyroid function tests were done for 112(71%) patients. T3, T4 and TSH assays were the common thyroid function tests done. Free T3 and Free T4 were assayed in only 15% of the patients.

The diagnosis was confirmed biochemically in 57% patients. Seventeen percent of the patients had normal thyroid function tests. Majority of these had been on anti thyroid drugs before presenting to KNH. Forty-five (29%) patients did not have TFTs records in their files.

Other tests done were:

Anti-thyroid antibodies; done in one patient. Reported as positive. ¹³¹I uptake studies were done for 9 patients. They were reported as high in 6, normal in 2, one was Graves' disease and another as thyroiditis.

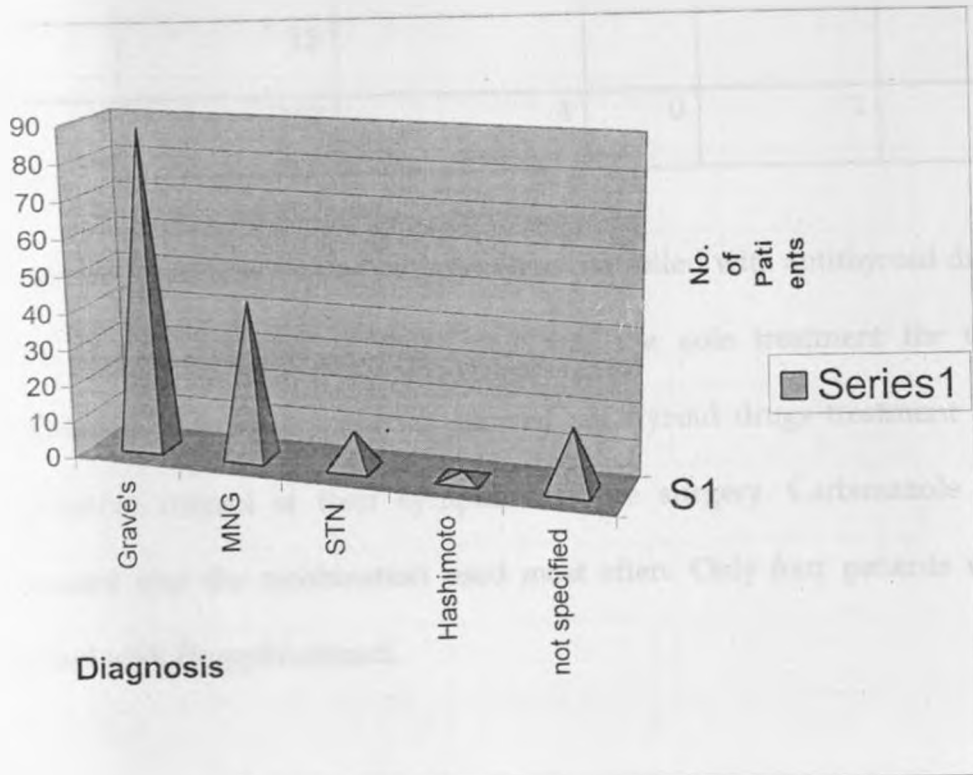
Histological diagnosis was available for 30 patients. Twelve are reported as benign disease, 7 multinodular goitre; 5 Graves' disease; 2 Hashimoto's thyroiditis and one had follicular carcinoma.

Fine needle aspiration cytology (FNAC) and ultrasound scan was done for 14 and 23 patients respectively. These did not add any significant information to the diagnosis.

DIAGNOSIS

The commonest cause of hyperthyroidism was Graves' disease, which was diagnosed in 88(55%) patients. Toxic multinodular goitre was diagnosed in 44(27%) patients while Solitary Toxic Nodule was diagnosed in 11(6%) patients. Hashimoto thyroiditis was seen in 2(1%) patients. Seventeen patients (11%) did not have a classified diagnosis.

Figure 7: Final Classification of various Toxic Goitres



Medical Management

Table 2: Duration of medical treatment

Duration	DRUGS				
	Carbimazole	Propylthiouracil	Iodine	Thyroxine	Propranolol
0-3 months	8	4	-	1	7
3-6 "	6				3
6-12 "	23				21
Not specified	52				43
None	13				13
Total	102	4	0	1	87

One hundred and thirty seven patients were controlled with antithyroid drugs initially. For Eighty-nine of these, this was the sole treatment for their thyrotoxicosis. Forty-four patients received antithyroid drugs treatment as a pre-operative control of their symptoms before surgery. Carbimazole and Propranolol was the combination used most often. Only four patients were controlled with Propylthiouracil.

Thirteen patients were discharged from the medical wards without starting treatment because of lack of antithyroid drugs. They were supposed to buy their medication as outpatients. There is no indication whether this was done.

Radioactive Iodine Treatment

Seventeen patients were treated with I¹³¹. Majority of these had failed medical treatment. Two patients of these received this form of treatment after histology showed that they had cancer of the thyroid after undergoing surgery for toxic goitre initially. Fifty-seven percent of the patients were euthyroid after one course, 36% required 2 courses and one became hypothyroid with one course of treatment.

Pre-operative medical management

Table 3: Duration of pre-operative medical treatment

Duration (months)	DRUGS		
	Carbimazole	Propranolol	Iodine
0-3	9	8	1
3-12	4	3	
6-12	21	21	
>12	2	2	
Not Specified	8	8	1
None	18	18	
Total	62	60	2

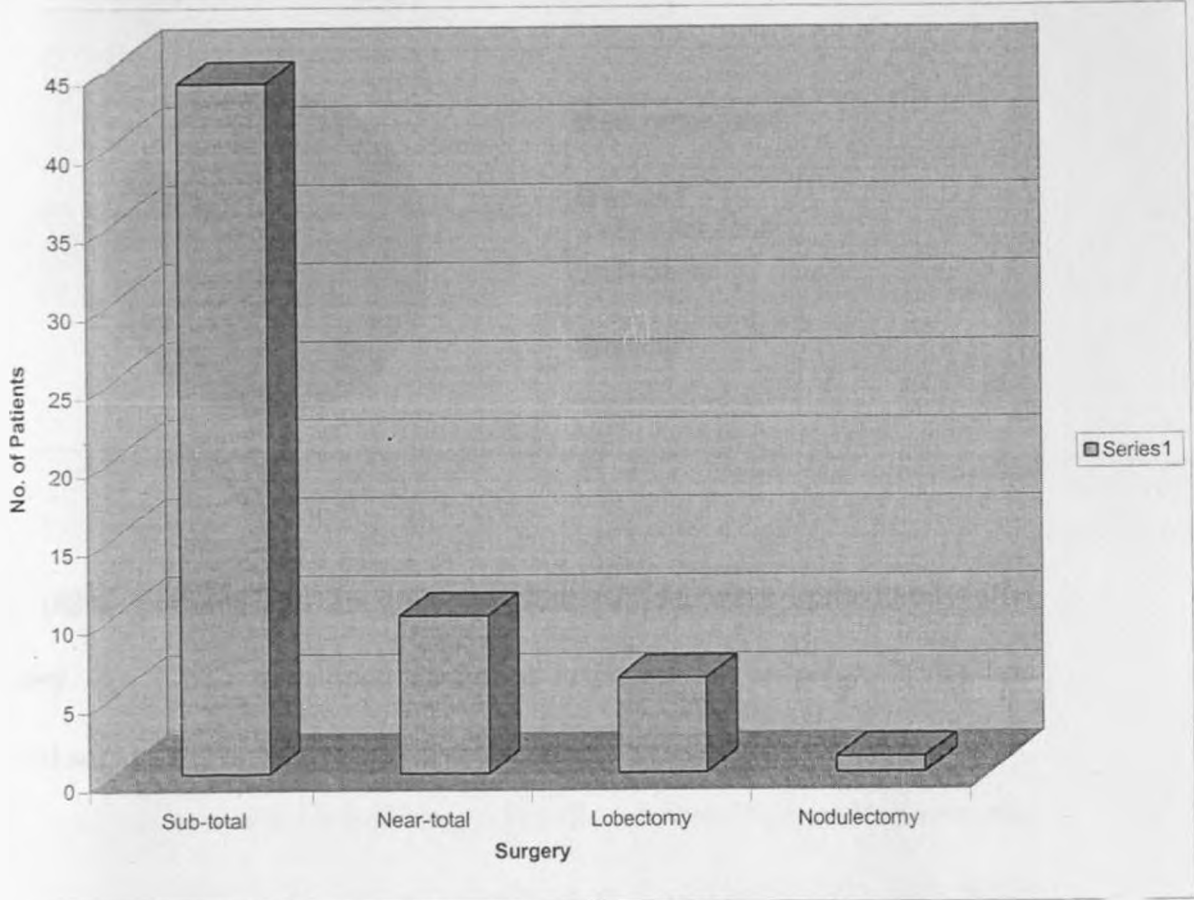
Of the 164 patients included in this study, 62 were treated surgically. Pre-operative control of thyrotoxicosis was achieved mainly with Carbimazole and propranolol. The duration of pre-operative control was 0-3 months for 9(20%), 3-12 months for 4(9%), 6-12 months for 21(48%) and more than 12 months in 2(5%) patients. The duration of pre-operative control of thyrotoxicosis is not indicated in 8(18%) of the 44 patients treated with antithyroid regime of carbimazole and propranolol in KNH clinics. The rest had been controlled in other clinics/hospitals and were only referred to KNH for surgery. Iodine was administered to 2 patients pre-operatively to correct over treatment with antithyroid regimes.

Postoperative Treatment

Post-operatively, 5 patients were treated with antithyroid drugs due to recurrence of thyrotoxicosis while another 5 were treated for hypothyroidism with thyroxine

SURGERY

Figure 8: Type of Thyroidectomy performed

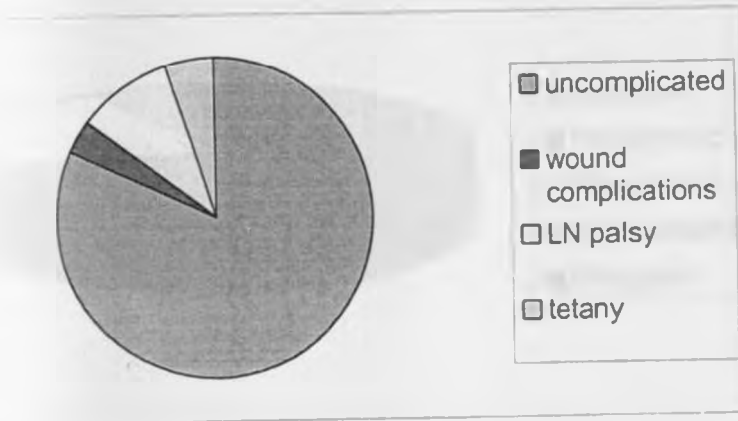


The most commonly performed surgery was subtotal thyroidectomy. Forty-four (71%) had this surgery while 10(16%) had a near total thyroidectomy performed on them. Seven (11%) patients had lobectomies done and nodulectomy was done in only one (2%) patient.

OUTCOME OF SURGERY

Immediate post-operative period

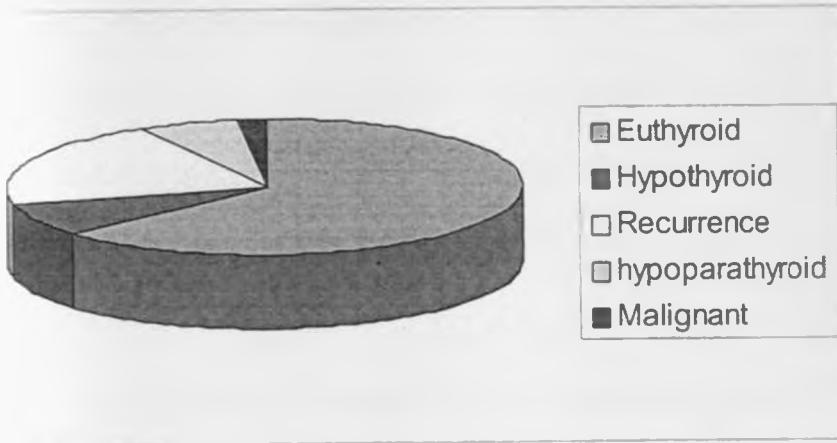
Figure 9: Post-operative Complications



Fifty (82%) patients had an uncomplicated/full recovery immediately after surgery. Six (10%) developed recurrent laryngeal nerve palsy, 2(3%) had wound sepsis and only 3(5%) got hypocalcaemic tetany.

LONG-TERM OUTCOME

Figure 10: Long-term Outcome of Surgery.



Upon discharge from hospital, patients were followed up in surgical outpatient clinics and the thyroid clinic. From the study group, 49(80%) were followed up for at least one year. 13(20%) were lost to follow up.

Of the patients available for follow up, 34(69%) remained euthyroid at one year after surgery. Ten (20%) had a recurrence of hyperthyroidism and 4(8%) became hypothyroid. Three (6%) patients developed chronic hypoparathyroidism while one patient had a malignant transformation, developing follicular carcinoma seven years after surgery.

In comparison, the patients treated with antithyroid drugs only had a higher recurrence rate. Seventy-three percent had uncontrolled thyrotoxicosis twelve

months after commencing treatment and only 27% remained euthyroid one year after treatment.

DISCUSSION

PREVALENCE

Thyroid diseases are the second commonest endocrine disorders seen in KNH, second only to diabetes mellitus. Most of these are benign enlargement of the thyroid gland. Between January 1991 and December 2000, 1206 patients with thyroid diseases were seen in KNH. Of these, only 356 had thyrotoxicosis. This is about 30% of all thyroid diseases.

The prevalence of thyroid diseases in KNH during this period is 1:1000, while that of toxic goitre is 3:10,000

The distribution of patients seen shows that the majority came from parts of Central and Eastern provinces neighbouring Nairobi i.e. Kiambu, Machakos and Thika districts. A sizeable number of patients came from the 'Highland' districts of Embu, Meru (in Central Province), Kisii and Nyamira (in Nyanza Province), Bomet, Kericho (in Rift Valley Province) and Kakamega in Western Province. This pattern mimics that of endemic goitre and could be due to relative iodine deficiency.

AETIOLOGY OF THYROTOXICOSIS

The epidemiological picture of thyrotoxicosis in KNH compares well with those reported in the west and elsewhere in Africa. Graves' Disease accounts for 55%,

toxic multinodular goitre 27%, solitary toxic nodule for 6% and Hashimoto's thyroidities less than 1%.

Toxic multinodular goitre's relative high prevalence in Africa, as reported here for KNH and by Ahmed ME²⁶ et al in Khartoum (34%), mimics that of endemic goitre, which is still prevalent in this region. This presents an opportunity for control of this disease by iodination of foods in the high-risk regions.

Graves' Disease affects a population ten years younger than toxic multinodular goitre. The average age for Graves' disease patients is 31 years, 41 years for toxic multinodular goitre and 33 years for solitary toxic nodule.

Toxic goitre is a predominantly female disease with a male to female ratio of 1:4.2.

MANAGEMENT OF TOXIC GOITRE IN KNH

The diagnosis of hyperthyroidism in KNH is based on the clinical presentation and thyroid function tests.

The main presenting complaints are: neck swelling, heat intolerance/excessive sweating, palpitations, weight loss, eye complaints and increased appetite.

Chief clinical findings are: goitre, tachycardia, ophthalmopathies, hypertension, tremors and warm moist peripheries.

Thyroid function tests were the investigations of choice. TSH, T3 and T4 assays were done for 70% of the patients. In most instances this confirmed the diagnosis. Free T3 and free T4 assays were not readily available and were assayed in only 15% of the patients. Anti-thyroid antibodies were assayed in only one patient while twenty-four patients had I¹³¹ uptake studies. Histological diagnosis was available for 50% of the patients treated surgically. Malignancy was diagnosed in one patient and two patients had Hashimoto's thyroiditis. Nine percent of the patients had fine needle aspiration cytology and 16% had ultra sound scans done. These latter two investigations did not add any significant information to the diagnosis.

TREATMENT

Medical treatment and pre-operative surgical management was with carbimazole and propranolol. Seventy-five percent of the patients received this treatment as compared to 2.5% who were managed with propyl thiouracil. Thirteen percent of the patients on medical treatment could not afford to buy their medication and left the wards without starting treatment while 75% in the same group were still toxic one year after start of treatment. Forty-five percent of those treated surgically took more than six months to control their symptoms

adequately to permit surgery to take place. The common denominator in all these cases is erratic drug compliance due to the cost of the drugs. Eight percent of the patients were treated with I¹³¹. Half of these were euthyroid immediately while the rest required a second dose to control their symptom.

Surgery was performed for 38% of the patients seen during the study period. Sub-total thyroidectomy was offered to 72% of the patients. Sixteen percent had near total thyroidectomy, 10% lobectomies and 2% nodulectomies.

Ajao OG et al³⁷ advocate the treatment of thyrotoxic patients as and when they present even if they are still toxic so long as thyroid crisis is anticipated and its occurrence is prevented by using saturated solution of potassium iodide (SSKI) or Lugol's iodine, propranolol, diazepam and hydrocortisone. Baeza A et al⁵⁶ in their study of rapid pre-operative preparation in hyperthyroidism also demonstrated that the use of betametasone, iopanoic acid and propranolol is safe, effective and of low cost and can be used in patients requiring urgent thyroidectomy or in those who need short preoperative regime. These two measures can also be adapted for our patients to shorten the preoperative period and improve compliance.

OUTCOME OF SURGERY

Eighty two percent (82%) of the patients treated surgically recovered fully from surgery. Ten percent developed recurrent laryngeal nerve palsy while another 5% had hypocalcaemic tetany due to removal of all their parathyroid glands. Only 3% developed wound complications such as sepsis or bleeding. The rate of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism is high compared to studies done elsewhere. Khandra M et al⁵⁷ in Australia report rates of 0.5% while Toropov Iud et al⁵⁸ study had incidence of 1%. The cause of this high incidence of RLN injury could be due to the large sizes of the goitres operated on or poor technique/inexperience of some of the surgeons.

Twenty percent (20%) of the patients who had surgery were lost to follow-up at one year. Of the remaining 80% who were followed-up for more than one year, 69% remained euthyroid. Twenty percent had recurrence of thyrotoxicosis and 8% became hypothyroid. Six percent developed chronic hypoparathyroidism. This compares favourably to patients managed medically whom only 27% were euthyroid one year after start of treatment.

The incidence of recurrence is high compared to the study of Torre G. et al²⁵ in Italy and Chiu MT et al⁵⁹ in Singapore. Torre G. found after ten years follow-up that 9% patients had developed recurrence while Chiu MT found one year after surgery that 84% of the patients remained euthyroid, 8% developed

hypothyroidism and 8% had relapsed thyrotoxicosis. Explanation for this lies with the large size goitre operated on and possibly the calibre of the surgeon doing the surgery.

Apart from poor drugs compliance, factors predicting outcome of medical treatment are not fully established. Some authors have suggested that high initial T3 levels or high freeT3/freeT4 ratios and presence of eye signs result most likely in failure of medical treatment. Tajiri J et al⁶⁰ (in Japan) found that FT3 toFT4 ratios ((FT3 (pg/ml)/FT4 (ng/dl) x10) were less than 55 for patients who remained in remission after antithyroid treatment whereas the ratios exceeded 55 from early phase of treatment in 75% of patients with relapse. de Rave S et al ⁶¹(in Netherlands) found that initial serum T3 levels and presence of eye signs as significant prognostic factors. These predictions can be used in the choice of therapy, medical treatment for low risk patients and surgery for high-risk patients.

CONCLUSIONS

Surgical management of hyperthyroidism in KNH affords a long-term control of the disease with a euthyroid status of more than 69% maintained at one-year follow-up. This is far more superior to medical management of the disease, which recorded only 27% euthyroid status after one-year treatment and follow-up

Efforts should be made to find the cause and remedy of the relatively high, 20% of recurrence of hyperthyroidism and recurrent laryngeal nerve and parathyroids injury.

With the spiralling cost of antithyroid drugs, poor medical treatment outcome and the good outcome of surgical care, surgery should be recommended to most of our patients early to achieve effective treatment of hyperthyroidism.

RECOMMENDATIONS

- 1 A protocol should be established in KNH for the management of thyrotoxicosis to standardize and optimise management options.
- 2 Surgery should be offered to most of our patients as the primary mode of treatment as this has a higher success rate at control of hyperthyroidism (69%) as compared to medical treatment (27%).
- 3 Thyroid function tests are the only necessary investigations to establish the diagnosis of thyrotoxicosis and other investigations should be ordered only when indicated.
- 4 A study is recommended to verify whether the findings of de Rave et al and Tajiri J et al are applicable in our setting so that the ratio of T3/T4, initial T3 levels and presence of eye signs could be used as an indication for surgery.
- 5 Pre-operative control of thyrotoxicosis should be optimised with close follow-up to shorten the waiting period before surgery. Alternative regimes like those used by Baeza A et al and Ajao OG et al could be adopted for rapid pre-operative preparation.
- 6 Audit of thyroid surgery in KNH should be done to establish the cause of the relatively high rates of recurrent laryngeal nerve palsy and recurrence of hyperthyroidism and remedial measures taken.

APPENDIX 1

Proforma Questionnaire

A ten-year retrospective study on the presentation, surgical management and outcome of hyperthyroidism in Kenyatta National Hospital (1991-2000)

Name: _____
IP. NO.:
Residence:
Province of origin:

Race:
African Asian Caucasian
Others (specify).....

Age at first presentation:

0-10 years	<input type="checkbox"/>	41-50 years	<input type="checkbox"/>
11-20 years	<input type="checkbox"/>	51 - 60 years	<input type="checkbox"/>
21-30 years	<input type="checkbox"/>	61 - 70 years	<input type="checkbox"/>
31-40years	<input type="checkbox"/>	> 70 years	<input type="checkbox"/>

Sex

Male

Female

Family history of hyperthyroidism

Yes

No

Date at first presentation:

Referred from another institution:

Yes

No

Referring institution

Health centre Private clinic

Mission Hospital Provincial Hospital

District Hospital Private Hospital

Others

(specify):.....

Symptoms at first presentation

Weight loss Restlessness

Malaise Tremors

Vomiting Diarrhoea

Onycholysis	<input type="checkbox"/> Irritability	<input type="checkbox"/>
Muscle weakness	<input type="checkbox"/> Chorea athetosis	<input type="checkbox"/>
Palpitations	<input type="checkbox"/> Heat intolerance	<input type="checkbox"/>
Eye complaints	<input type="checkbox"/> Neck swelling	<input type="checkbox"/>
Oligomenorhea	<input type="checkbox"/> Loss of libido	<input type="checkbox"/>
Gynaecomastia	<input type="checkbox"/> Tall stature	<input type="checkbox"/>

Findings on physical examination (Signs)

Weight loss	<input type="checkbox"/> Tremors	<input type="checkbox"/>
Irritability	<input type="checkbox"/> Hyperkinesia	<input type="checkbox"/>
Ophthalmoplegia	<input type="checkbox"/> Exophthalmos	<input type="checkbox"/>
Lid lag	<input type="checkbox"/> Systolic hypertension	<input type="checkbox"/>
Cardiac failure	<input type="checkbox"/> Atrial fibrillation	<input type="checkbox"/>
Tachycardia	<input type="checkbox"/> Thyroid acropachy	<input type="checkbox"/>
Onycholysis	<input type="checkbox"/> Palmer erythema	<input type="checkbox"/>
Psychosis	<input type="checkbox"/> Goitre	<input type="checkbox"/>
Warm dilated periphery	<input type="checkbox"/> Pretibial Myxaedma	<input type="checkbox"/>
Proximal muscles wasting	<input type="checkbox"/>	

Investigations done:

Laboratory Investigations:

Thyroid function tests

	Normal	Low	High	Very High (>3x normal)
T4				
T3				
Free T4				
Free T3				
TSH				
TRH				

T3 suppression test

Positive

Negative

Anti-thyroid antibodies

Positive

Negative

Erythrocyte Sedimentation rate

Normal

Low

Haemoglobin level (g/dl)

< 10 10 - 12 > 12

Ultra Sound Scan:

Diffuse: Homogenous Inhomogeneous

Cystic: Simple Degenerative changes

Multiple nodules Solitary nodules

Volume of the gland

~20cc 20-50c >50cc

Position of the gland

In the neck Retrosternal

Fine Needle Aspiration Cytology

Normal Benign disease

Malignant disease

Radioisotope uptake studies:

Low Normal High

Other Investigations

	Normal	Abnormal (Specify)
ECG		
CXR		
Thoracic inlet view:		
CT Scan:		

Preoperative Complications Specify):.....

.....
.....

Diagnosis:

Graves' disease Multi nodular

goitre

Solitary thyroid

nodule

Others (specify):.....

.....
.....

Management

Medical management

As a choice	<input type="checkbox"/>	Pre-op	<input type="checkbox"/>
Post-op	<input type="checkbox"/>		

Pre-operative medical management

Drug	Duration			
	0-3/12	3-6/12	6-12/12	>12/12
Carbimazole				
Propyl thiouracil				
Propranolol				
Iodine				
Thyroxine				

Others (specify):.....

.....

.....

Postoperative medical management

Drug	Duration			
	0-3/12	3-6/12	6-12/12	>12/12
Carbimazole				
Propyl thiouracil				
Propranolol				
Iodine				
Thyroxine				

Others (specify):.....

Radioiodine treatment

As a choice Pre-op
 Post-op

Surgical treatment

Sub-total Near-total
 thyroidectomy thyroidectomy
 Lobectomy Nodulectomy
 Total
 thyroidectomy

Outcome of surgery:

Immediate

Uncomplicated

Complicated

Wound complications

Haemorrhage

Laryngeal nerve palsy

Thyroid crisis

Hypocalcaemic tetany

Death

Long-term outcome

Hypothyroid state

Hyperthyroid state
(recurrence)

Euthyroid state

Hypo parathyroid
state

APPENDIX 2

REFERERNCES:

1. Reverdin, D. Berker, G. Konig, MP. Rinchera, A. Schalz, H. Schlenner, A. The different types of hyperthyroidism in Europe: Results of a prospective study of 924 patients. *Journal of endocrinology investigation*. 1988; **11**:193
2. Trzepak, PT. Klien, I.. Robert, M. Greenhouse, J. Levey, GS. Graves disease an analysis of thyroid hormones levels and hyperthyroid signs and symptoms. *American Journal of Medicine* .1989; **87**: 558
3. Lewis, E. Braverman, Robert D. Utiger. Introduction to thyrotoxicosis in: *The thyroid a clinical and fundamental text (Sixth edition)*(1991) J.B. Lippincort company. **30**:645
4. Rollenstone, HD. The endocrine organs. In: *Health and disease*. London. *Oxford University Press*. 1936; **3**:10.
5. Thompson, J. Historical Notes, in: Smither's D.Ed. Tumours of the thyroid *Neoplastic diseases at various sites. (Vol.6) Edinburgh: Churchill Livingstone*, 1970.**2**:12.
6. Suttler, H. Base Dow's disease. *New York: Grune and Stratton*, 1952
7. Sidney C. Werner. History of the thyroid, in: *The Thyroid a clinical and fundamental text (sixth edition) Lippincot company* 1991; **1**: 3.
8. Eustachius B. In: Rollenstone HD: *Health and Disease*, London. *Oxford Press*. 1936; **152**.

9. **Cooper, AP.** Notes on the studies of the thyroid gland. *Guys Hospital Report.* 1836; 1:448.
10. **King, TW.** Observations on the thyroid gland. *Guys Hospital Report.* 1836; 1:429.
11. **Reverdin ,JL. Reverdin, A.** Note sur vingtdex operations de goitre. *Rev. Med Suisse Romande .*1883. 3: 169.
12. **Kocher, T.** Ueber kropfsextirpatin und ihre folgen. *Arch Klin Chir .*1883; 29:254.
13. **Parry, CH.** Collections from the unpublished papers of the late Caleb Hilhel Parry Vol2 London. 1825; 111.
14. **Graves ,RJ.** Clinical lectures. *London medical surgery journal.*1835; 7:516.
15. **CA Von Basedow.** Exophthalmos durch hypertrophie des zellgewebes in der Augenhoteile. *Wochenschr heilk.*1840; 6:197.
16. **Rehn, L.** Ueber die extirpation ds kropfs bei morbus Basedowii. *Klin. Wochenschr.*1884; 21:163.
17. **Magnus Levey.** a ber den respiratorischen Gasweschel unter den einfluss der Thyroidea sowie unter Verschieenen Pathologischen Zustnden. *Klin Woncherschr.* 1895; 32:650.
18. **Moore, KL. Persard, TUN.** Development of the thyroid gland, in: *The developing human. (Sixth edition) WB Saunders Co.* 1998; 10:230.
19. **Janquira, LC. Canneiro, J. Kelley, PO.** Thyroid Histology in: *Basic Histology (eight edition) Lange Medical Book.* 1997; 21:399

20. **Ganong, FW.** The thyroid gland, in: *Review of Medical Physiology (nineteenth edition)*. 1999; **18**:303,304,309.
21. **Volpe Robert.** Graves Disease, in: *The Thyroid a clinical and fundamental text*. Lippincot Company. 1991; **31**:648.
22. **Struder, H. Gerber, H. Peter, HJ.** Multinodular Goitre, in: *De Groot LJ, Ed. Endocrinology (second edition) Philadelphia; WB Saunders* .1989: 722.
23. **Plummer, HS.** The clinical and pathological relationship of simple and exophthalmic goitre. *American Journal of Medical Science* .1913; **146**:790.
24. **Hay, ID. Morris, JC.** Autonomously Functioning Thyroid Nodules, in: *Werner and Ingbars; the Thyroid, a clinical and fundamental text. (sixth edition)* 1991; **698**:701.
25. **Torre, G. Borgonuvo, G. Arrezo, A. Constantini, M. Varaldo, E. Ansaldo, GL. Mattioli, FP.** Is euthyroidism the goal of surgical treatment of diffuse toxic goitre? *European journal of surgery*. July 1998; **164**(7): p495-500.
26. **Ahmed, ME. Elwasila, AA. Sarhomi, M. Yagi, K.** Surgical management of toxic goitre in Khartoum. *Trop. Geogr. Med.*. 1993; **45**(3): p124-5.
27. **Crooks, J. Murray, IPC. Wayne, EJ.** Statistical methods applied to the clinical diagnosis of thyrotoxicosis. *QJ Med*. 1959; **28**:21.
28. **Trzepacz, PT. Klein, I. Roberts, M. Greenhouse, J. Levey, GS.** Graves disease: an analysis of thyroid hormone levels and hyperthyroid signs and symptoms. *American journal of medicine*.1989; **87**:558.

29. Surks, MI. Chopra, IJ. Mariash, CN. Nicoloff, JT. Solomon, DH. American Thyroid Association guidelines for use of laboratory tests in thyroid disorders. *JAMA*. 1990; 263: 1539.
30. Astwood, EB. Treatment of hyperthyroidism with thiourea and thiouracil. *JAMA*. 1943; 122: 78.
31. Taurog, A. Mechanism of action of the thiouracyl antithyroid drugs. *Endocrinology (oxford)*. 1976; 98:103.
32. Volpe, R. Kurlson, A. Jansson, R. Dahlberg, PA. Evidence that antithyroid drugs induce remissions in Graves' disease by modulating thyroid cellular activity. *Clinical Endocrinology (oxford)*. 1986; 25:453.
33. Janson, R. Dahlberg, PA. Lindston, B. Comparative bioavailability of carbimazole and methimazole. *Journal of clinical pharmacology therapy and toxicology*. 1983; 21:505.
34. Young, ET. Steel, NR. Talor, JJ. et al. Prediction of remission after antithyroid drug therapy in Graves' disease. *Queen's Journal of Medicine*. 1988; 250:175.
35. Down, JT. Choice of therapy in young adults with hyperthyroidism of Graves' disease. A brief case directed poll of 54 Thyroidologist. *Annals of Internal Medicine*. 1984; 100:891.
36. Solomon, B. Glinar, D. Lagasse, R. Wartofsky, L. Current trends in the management of Graves' disease. *Journal of Clinical Endocrinology Metab*. 1990; 70:158.

37. Ajao, O. Soyannwo, OA. Adebamawo, CA. Okeke, LI. Ladipo, JK. Sotumbi, PT. Surgery of toxic goitre in non-euthyroid patients: a preliminary report. *African Journal of Medicine and medical care*. 1997; 26(1-2): 59-62.
38. Hedley, AI. Young, RE. Jones, SJ. Alexander, WD. Bewsher, PD. Antithyroid drugs in the treatment of hyperthyroidism of Graves' disease: long-term follow-up of 434 patients. *Clinical Endocrinology (oxford)*. 1989; 31:209.
39. Feely, J. Stevenson, IH. Crooks, J. Increased clearance of propranolol in thyrotoxicosis. *Annals of internal medicine*. 1981; 94:127.
40. Feely, J. Peder, N. Use of β -adrenoceptor blocking drugs in hyperthyroidism. *Drugs*. 1984; 27; 245.
41. Beckler, DV. Choice of therapy for Graves' hyperthyroidism. *New England Journal of Medicine*. 1984; 311:464.
42. Dailey, ME. Lindsley, S. Miller, ER. Histologic lesions in the thyroid glands of patients receiving radioiodine for hyperthyroidism. *Journal of clinical Endocrinology metab*. 1953; 13:153.
43. Holm, LE. Lundell, G. Dahlqvist, I. Israelson, A. Cure rate after I^{131} therapy for hyperthyroidism. *Acta. Radiology*. 1981; 20:161.
44. Graham, GD. Bunman, KD. Radioiodine treatment of Graves' disease. *Annals of internal medicine*. 1986; 105:900.

45. Kleintschitsch, P. Sheu, K. and Kaplan, EL. Re-emergence of thyroidectomy as a treatment for Graves' disease. *Lancet*. 1976; 1:603.
46. Sugrae, D. McEvoy, M. Feely, J. Drury, MI. Hyperthyroidism in the lands of Graves: results of treatment by surgery, radioiodine and carbimazole in 837 cases. *Queen's journal of medicine*. 1980; 49:51.
47. Toft, AD. Irvine, WJ. Sinclair, I. McIntosh, D. Seth, J. Cameroon, EHD. Thyroid functions after surgical treatment of thyrotoxicosis. *New England Journal of Medicine*. 1978; 298:643.
48. Hedley, AJ. Brewshew, PN. Jones, SJ. et al. Late onset hypothyroidism after sub-total thyroidectomy for hyperthyroidism: Implications for long-term follow-up. *British Journal of Surgery*. 1983; 70:740.
49. Reid, DJ. Hyperthyroidism and hypothyroidism complicating therapy of thyrotoxicosis. *British Journal of Surgery*. 1987; 74:1060.
50. Kalk, WJ. Durbach, P. Kartor, S. and Levin, J. Post-thyroidectomy thyrotoxicosis. *Lancet*. 1978; 1:291.
51. Lennquist, S. Jortso, E. Anderberg, BO. Sneede, S. β -blockers compound with anti-thyroid drugs as pre-operative therapy in hyperthyroidism: Drug tolerance, complications and post-operative thyroid functions. *Surgery*. 1985; 98:141.
52. Terscher, J. Peter, HJ. Gerber, H. Berchtold, R. and Struder, H. Pathogenesis of nodular goitre and its implications for surgical management. *Surgery*. 1988; 103:87.

53. **Hamburger, JI.** Evolution of toxicity in solitary non-toxic autonomously functioning thyroid nodule. *Journal of clinical Endocrinology Metab.* 1980; 50:1089.
54. **Hempelman, LH.** Risk of thyroid neoplasm after irradiation in childhood. *Science.* 1968; 160:159.
55. **Fontana, B. Curti, G. Biggi, A. et al.** The incidence of hypothyroidism after radioiodine (I^{131}) therapy for Autonomously functioning thyroid nodules evaluated by life tables method. *New England Journal of Medicine.* 1983; 309:1473
56. **Baeza, A. Aguayo, J. Barria, M. Rinada, G.** Rapid preoperative preparation in hyperthyroidism. *Clinical Endocrinology (oxford)(England).* Nov.1991; 35(5): p439-42.
57. **Khandra, M. Delbridge, L. Reeve, TS. Poole, Ali. Crummer, P.** Total thyroidectomy, its role in the management of thyroid disease. *Australia /New Zealand Journal of Surgery (Australia).* Feb.1992; 62(2): p91-5.
58. **Toropov, Iud. Izbitskii, Vi.** The surgical treatment of patients with thyrotoxic goitre. *Klin Khir.* 1991; 12: p19-22.
59. **Chiu, MT. Soon, PC. Ng, PK.** Selection of patients for surgery in management of thyrotoxicosis. *Annals of the Academy of Medicine, Singapore.* July 1993; 22(4): p553-6.

MEDICAL LIBRARY
UNIVERSITY OF NAIROBI

60. Tajiri, J. Nogachi, S. Moritu, M. Tanaru, M. Murakami, N. Kato, R. Serum free T3: free T4 ratio enables early prediction of the outcome of antithyroid drugs treatment in patients with Grave's hyperthyroidism. *Endocrinology Japan (Japan)*. Dec.1991; 38(6): p683-7.
61. De Raves, S. Goldschmidt, HM. Bravenboer, B. Loosveld, OJ. Lockerfeur, JH. Logistic multiple regression analysis of factors predicting recurrence of hyperthyroidism after medical treatment of toxic diffuse goitre. *Netherlands Journal of Medicine (Netherlands)*. Oct.1991; 39(3-4): p131-5.