THYROID-ASSOCIATED EYE DISEASE IN PATIENTS WITH THYROID DISEASE ATTENDING THYROID CLINIC AT THE KENYATTA NATIONAL HOSPITAL

A DISSERTION SUBMITTED IN PART FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE (OPHTHALMOLOGY) AT THE UNIVERSITY OF NAIROBI.

BY

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Declaration and approval

This dissertation is my original work and has not been presented for a degree in any other University.

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Dedication

This book is dedicated to my family, for their unswerving support, inspiration, great optimism and patience.

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Acronyms and abbreviations

KNH-Kenyatta National Hospital

TAED-Thyroid associated eye disease

SPSS-Statistical package for social scientists

TFTs-Thyroid function tests

%-Percentage

CDR-Cup disc ratio

HR-Hypertensive retinopathy

VF-Visual fields

ABSTRACT

The aim of this study was to determine the epidemiology of TAED, its manifestations, complications and treatment as seen in KNH.

It was a cross-sectional study conducted in patients attending the thyroid clinic of KNH. Data was analyzed using SPSS version 10.

A total of 111 Africans of Kenyan origin were examined. 103 of them were females and 8 were males. The age range was from 7 to 80 years.

TAED was present in 64 of 111 patients giving a prevalence of 58%. Eighteen of them had had thyroidectomy and 29 were on antithyroid drugs. Fifty seven (89%) of patients were diagnosed to have thyroid disease in the medical clinic, but 7 (11%) of them first presented to the eye clinic with symptoms attributable to TAED and were then referred to the physician. Eleven (17%) had severe form of the disease while 53 (83%) had non-severe disease. Only 7 of the patients who had severe disease had active disease. Sixty two (97%) patients had bilateral disease and only 2 (3%) had unilateral disease.

The common presenting complaints were redness and foreign body sensation. Most of the patients had multiple complaints. Five patients complained of double vision.

The most common signs were conjuctival injection, lid retraction and proptosis in that order. Two patients had constant diplopia and one of them had a chin lift. Five patients had exposure keratitis due to marked proptosis. Three patients were found to have optic

atrophy but no patient had choroidal striae. One patient was found to have hypertensive retinopathy grade two.

22 patients were on various treatments for TAED. Sixteen patients were on topical steroids. One patient was on patching therapy for diplopia while another had tarrsorhaphy to prevent exposure keratopathy. Two patients were on artificial tears for dry eyes and exposure keratopathy. No patient had decompression, radiotherapy or extraocular muscle surgery done.

INTRODUCTION

(a) Background of the study

Thyroid associated eye disease is a common problem. Complications associated with it have a major impact on physical, emotional and social well being of the patient. Graves disease is by far the commonest cause of thyroid associated eye disease. It was first described by Sir Robert James Grave in 1835 in Dublin (1).

This study is designed to determine the prevalence of ocular involvement, manifestations, complications and treatment of this disease as seen in patients attending thyroid clinic of Kenyatta National Hospital.

A similar study was done by Godfrey Obonyo in 1988. In his study, he reported a very high prevalence (76.9%) of thyroid associated eye disease in Kenyatta National Hospital. The documented prevalence in other populations is varied but ranges from 25 – 50%. In view of this disparity, this study is to verify if indeed there is such a high prevalence by careful selection of patients. The previous study having been done over a decade ago, it is probable that the prevalence may have changed over the past ten years.

The classification has changed over the years from NOSPECS (used by Godfrey Obonyo) to grading by disease activity and severity. These are clinically oriented and they influence the choice of treatment. NOSPECS is directed towards the mean status of the eye and it is difficult to evaluate isolated components separately. It has therefore been discounted. This change in classification has changed the overall management of patients. It will be interesting to compare the recent trends in the management of these patients.

(b) Classification

A classification of eye signs according to the type of involvement (1) with a mnemonic NOSPECS Standing for: -

- N No signs
- O Only signs
- S Soft tissue involvement
- P Proptosis
- E Extraocular muscles
- C Corneal involvement
- S Sight loss

Currently grading is based on disease severity and activity. Both influence the choice of treatment.

(a) **Assessment of severity**

	PARAMETER		
Degree of involvement	Proptosis (mm)	Diplopia	Optic neuropathy
Mild	19-20 (1-2)	Intermittent	Sub-clinical
Moderate	21-23 (3-4)	Inconstant	Visual acuity (6/9-6/12)
Marked	>23 (>5)	Constant	Visual acuity (<6/12)

Table 1: Disease severity (2)

Definition of terms.

I. Severe ophthalmopathy: - At least one marked, or two moderate, or one moderate and two mild manifestations.

II. Diplopia: - intermittent, present only when fatigued; inconstant, present in secondary positions of gaze; constant, present in primary and reading positions.

III. Sub clinical neuropathy: - in the absence of decreased visual acuity optic neuropathy is established by visual fields, colour test, CT scan or abnormal visual evoked potentials.

(b) Assessment of activity

To assess the activity of ophthalmopathy Mourits et al (3), proposed a clinical activity score (CAS). This has since been revised to contain seven parameters as shown below in the table 2 below.

PARAMETER	SCORE
Spontaneous retrobulbar pain	1
Pain on eye movements	1
Eyelid erythema	1
Conjuctival injection	1
Chemosis	1
Swelling of the caruncle	1
Eyelid edema or fullness	1
TOTAL SCORE	7

Table 2: Disease activity (3)

The range of the score varies from 0 (no activity) to 7 (greatest activity).

A score of 4 or more indicates active eye disease.

(c) Criteria of diagnosis

Clinically a patient with Graves disease presents with a triad of true hyperthyroidism, ophthalmopathy and dermopathy (4).

Hyperthyroidism

True hyperthyroidism is the commonest component of Graves disease (1). In true hyperthyroidism, thyrotoxicosis develops as a result of excessive thyroid gland synthesis and release of thyroxin (T4). The resulting hyperthyroidism is characterized by progressive enlargement of the thyroid gland (goitre) and elevated radioiodine uptake on nuclear scanning (>30% up to 90% in 24 hours). The goitre associated with thyroid eye disease is asymmetric, diffuse and non-tender. Large goitres tend to be vascular and a bruit is heard on auscultation (7).

The biochemical diagnosis of thyrotoxicosis requires the combination of suppressed thyroid stimulating hormone levels and elevated thyroid hormone concentrations. A few patients present with ophthalmopathy but without hyperthyroidism or goitre (euthyroid Graves disease). Others are hypothyroid as seen in hypothyroid Hashimotos disease (4,5). Salvi et al (6) reported that approximately 10% of patients with ophthalmopathy did not have hyperthyroidism but majority had laboratory evidence thyroid autoimmune disease.

Normal levels of thyroid function tests

(Kenyatta National Hospital, immunology laboratory-DRG Diagnostics)

Thyrotropin	0.4-6.2 microIU/ML
T4	4.4-11 micrigrams/dl
T3	0.69-2.02 ng/dl
Free T4	0.8-2.3 μg/dl
Free T3	1.38-4.04 μg/dl

Ophthalmopathy

The presence of ophthalmopathy in a thyrotoxic patient confirms Graves disease though its absence does not exclude it. It is the most frequent extrathyroidal manifestation of Graves disease (2).

Only about 5% of patients with Graves disease have obvious ophthalmopathy. In addition only a minority develop severe expression of the disease, requiring aggressive treatment (2).

The eye signs may appear long before the disease onset, with the disease or years after the disease has been treated (5).

Dermopathy

This almost always occurs in patients with severe ophthalmopathy. It is characterized by thickening of the dermis, pretibial myxedema, onycholysis and acropathy. It appears as a nodular or diffuse thickening of the skin of anterior lower leg but can occur elsewhere (7).

I EPIDEMIOLOGY

Graves disease is the commonest cause of hyperthyroidism occurring in 60-80% of patients with hyperthyroidism. Occurrence of Graves disease and Graves ophthalmopathy is concurrent since careful evaluation of these patients reveals ocular involvement in majority of patients (2,6).

Graves ophthalmopathy appears before Graves hyperthyroidisn in 20% of patients, simultaneously in 40% and 40% after Graves hyperthyroidism. A study by Marccoci et al (5) reported that regardless of which occurs first the other develops within 18 months in 85% of affected patients.

This disease can occur at any age and in all races .The prevalence of graves disease is similar among Whites and Asians and lower in Blacks. Clinically apparent ophthalmopahty occurs in 25-50 % of patients with hyperthyroid Graves disease.

Graves disease has symptomatic annual incidence of 0.5 /1000 women. It occurs 5-10 times more in women than men (8). The peak incidence is the fourth decade of life. It is unusual in children. Only 1-5 % of Graves disease patients are less than 15 years of age and this accounts for 10-15% of all childhood thyroid disorders (2,9,10,11).

II PATHOPHYSIOLOGY OF THYROID EYE DISEASE

i. *Physiology of Thyroid Hormone regulation*

Regulation of thyroid hormone is effected by two mechanisms (7).

(a) In the suprathyroid level, the mediator is thyroid stimulating hormone (TSH), a glycoprotein secreted by basophilic (thyrotrophic) cells in the anterior pituitary gland. TSH stimulates synthesis and secretion of thyroid hormone. Regulation of TSH secretion in turn is effected by thyrotropin releasing hormone (TRH), a tripeptide of hypothalamic origin. Thyroid hormone inhibits TSH secretion directly and antagonises the action of TRH by decreasing the number of receptors in the thyrotropic cells.

(b) In intrathyroid regulation (autoregulation), thyroid hormone synthesis is controlled by availability of organic iodine.

The regulation is shown in the diagram below: -

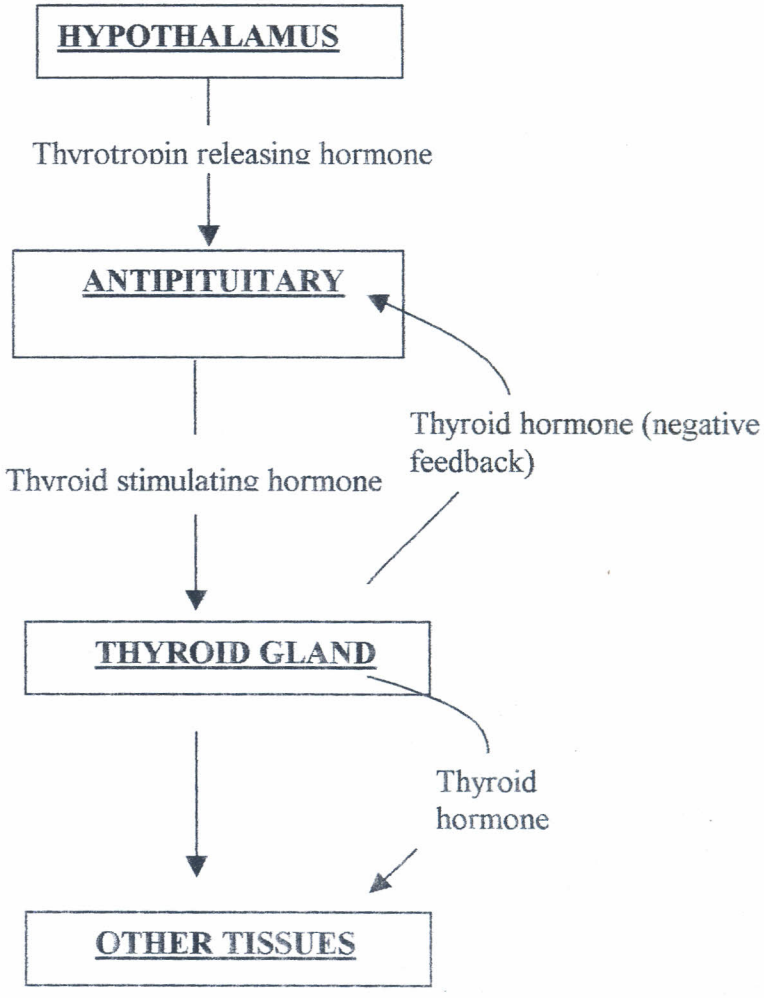

Diagram 1: Thyroid hormone regulation

ii Pathogenesis

When it was discovered in the 19th Century, Graves disease was thought to be an emotional problem because patients presented with tremor and palpitations. Extensive research shows that several factors may be involved in the pathogenesis of Graves opthalmopathy. These are thyroid stimulating hormone, ophthalmotropic factor and long acting thyroid stimulator (7).

It is now established that Graves ophthalmopathy is an autoimmune disorder (4). Circulating T-cells in patients with Graves disease are directed against an antigen shared by thyroid, orbit and pretibial skin. When they recognize this antigen, the T-cells infiltrate the orbit and pretibial skin (12, 13). Macrophages and plasma cells also infiltrate the orbital contents.

An interaction between the activated CD4 T cells and local fibroblasts results in release of cytokines into surrounding tissue (13).

The cytokines then stimulate the expression of immunomodulatory proteins in orbital fibroblasts thus perpetuating the autoimmune response in connective tissue (13).

In addition, cytokines stimulate proliferation of fibroblasts as well as glycosaminoglycan production by fibroblasts (13,14).

Glycosaminoglycans are hydrophilic macromolecules that bind water, causing increase in connective tissue volume.

Current research suggests the thyrotropic receptor to be the antigen causing ophthalmopathy (13, 15).

Histological and experimental evidence points to orbital and skin fibroblasts as the primary autoimmune targets in Graves ophthalmopathy and pretibial dermopathy respectively (13, 14).

iii Histology.

The increase in volume of tissue within the orbit is the proximate cause of many clinical manifestations of Graves ophthalmopathy.

Histological examination shows accumulation of glycosaminoglycans and inflammatory cells in the connective tissue components of orbital fats and muscles (13,14). Binding of water to the hydrophilic macromolecules is one cause of the increased volume in the orbits. In addition urinary glycosaminoglycan excretion is increased in patients with Graves ophthalmopathy suggesting generalized stimulation of glycosaminoglycan production by fibroblast throughout the body (16).

The accumulation of the glycosaminoglycan (14) and the infiltrating cells results in enlargement of extraocular muscles and surrounding fat (12,13). The muscle cells themselves remain intact (17,18). However they are widely separated by increased amount of connective tissue and the hydrophilic extracellullar matrix components. In the late stages extraocular muscles become fibrotic and atrophic due to chronic compression of the muscle fibers (13).

Exophthalmos occurs as result of increased volume of tissue in the bony orbit. Swelling of the extraocular muscles at the apex of orbits and lack of forward mobility of orbital contents due to tight attachment of connective tissue to the orbital walls (19) causes ischaemic optic neuropathy (19).

Chemosis and periorbital oedema are caused by decreased venous drainage from the orbit and by the orbital inflammation (2).

III MANIFESTATION OF THYROID ASSOCIATED EYE DISEASE

Majority of Graves patients have mild and non-progressive ocular involvement that does not require any specific or aggressive treatment (2). Non-severe Graves ophthalmopathy tends to improve spontaneously. In 10 – 25% of cases of ocular involvement, there is absence of both clinical and biochemical evidence of thyroid dysfunction (20). In this study, Bartley et al (21) found that out of 120 patients with Graves ophthalmopathy, 74% required no treatment or only supportive measures.

Two types of manifestation may occur in thyroid eye disease (22,23)

(1) Non-infiltrative ophthalmopathy.

(2) Infiltrative ophthalmopathy.

(1) Non-infiltrative ophthalmopathy

Patients with non-infiltrative ophthalmopathy have widening of the palpebral fissure, lag of the globe on upward gaze as well as lag of upper lid on downward gaze. These cause the sclera to be abnormally visible making the eyes appear exophthamic. In addition, there is lid retraction in majority of patients. This was been confirmed by Bartley et al (24) in a study on clinical features of Graves ophthalmopathy. They found eyelid

retraction occurring in 91% (108 out of 119). Lid retraction is chemically induced by overreaction of Müller muscle. This is as a result of sympathetic over stimulation secondary to high levels of thyroid hormone (25).

Non-infiltrative ophthalmopathy may have some undesirable cosmetic effects but carry no hazard to ocular function.

The features of this form of ophthalmopathy generally improve with treatment of hyperthyroidism (7, 10).

(2) Infiltrative ophthalmopathy

This is a unique characteristic feature of Graves disease which may co exist with non infiltrate ophthalmopathy.

(1) Soft tissue involvement

a) Lids

The lids are oedematous and erythmatous. This is caused by infiltration behind the orbital septum (20). The swollen lids usually feel firm and do not pit. There may be associated prolapse of retro orbital tissue into the eyelids further worsening the oedema (20).

Eyelid retraction in both infiltrative and non-infiltrative ophthalmopathy is responsible for functional and cosmetic problems. It may cause permanent conjuctival irritation and corneal complications.

Contraction of levator and inferior rectus muscles associated with fibrosis and local adhesions induce retraction of upper and lower lids respectively (20).

Secondary overreaction of levator-superior rectus complex in response to hypophoria produced by fibrosis and tethering of inferior rectus muscle is a cause of upper lid retraction. Similarly fibrosis of superior rectus muscle may induce retraction of inferior rectus muscle and hence retraction of the lower lid (26).

b) Conjuctival chemosis

There is chemosis and injection of scleral conjuctiva (7). It may be so severely oedematous to prolapse beyond the palpebral fissure. Associated hyperemic is a sensitive sign of disease activity. Due to prolapse and inability to close the lids may result in superior limbic keratoconjuctivitis and is usually bilateral. This is characterized by papillae in superior tarsal conjuctiva and hyperemia of superior bulbar conjunctiva. In addition, papillary hypertrophy of the limbus, puntate epitheliopathy and filaments of superior cornea may be present (20).

c) Lacrimal gland

The lacrimal gland can be totally destroyed by the infiltrative lesion. It may be enlarged and palpable and even visible. As a result keratoconjuctivitis sicca develops. Commonly therefore, the patient will complain of eye pain, irritation and grittiness of the eyes (27).

(2) Exophthalmos

Thyroid associated eye disease is the commonest cause of both unilateral and bilateral proptosis in adults (20,27). Bartley et al (24) noted that of the 120 patients, 62% presented with proptosis. A globe is proptosed when the anterior border of the cornea protrudes more than 20 mm beyond the lateral margin of the orbit. A difference of 2 mm between the two eyes is suspicious regardless of the absolute value (20). Often the globes cannot be easily displaced backward by digital pressure, the retrobulbar tissue being firm and unyielding. This is because of increase in volume of orbital

contents including fatty tissue and muscles (12, 13, 14). The prolapse of the globe beyond the palpebral fissure in extreme proptosis may permit a startling closure of the lids behind the globe.

The proptosis is axial and the patient has a staring and frightened facies (7, 27). In severe proptosis inadequate closure of the lids results to exposure keratopathy, corneal ulceration and endophthalmitis if not managed early enough (20). More often this presents a cosmetic challenge to the patient.

(3) Infiltration of the extraocular muscles

These muscles become infiltrated, inflamed and hypertrophy mainly due to increase in glycosaminoglycans (10,16,27). In some cases the muscles become enlarged to eight times their normal size (20). Hypertrophy at the apex may compress the optic nerve (20, 27).

The initial inflammatory lesion is followed by gradual recovery then fibrosis and later atrophy. Often the scarred and fibrotic muscles cause a fixed strabismus that persists indefinitely unless corrected surgically. This is known as restrictive myopathy and between 30-50 % hyperthyroid patients develop ophthalmoplegia (20). The diplopia may be transient but in 50% of patients it may be permanent. The extraocular muscles function is assessed by Hess charts.

Paralysis or paresis of the muscles occurs and upward gaze is affected first and most seriously with loss of convergence being common. Oculomotor paralysis may be severe when exophthalmos is minimal or absent (2). The insertion of the swollen

lateral rectus muscle is often visible at the outer canthus. This is obvious when the patient turns the globe medially and is a characteristic sign in Graves ophthalmopathy. The muscle enlargement can be recognized by ultrasound, CT scan and MRI (10). The enlargement is pathognomic of Graves disease.

(4) Increased intraorbital pressure

This occurs in 25% of patients with infiltrative thyroid eye disease (28). It was noted in clinical studies that upon up gaze an increase in intraorbital pressure correlated with severity of infiltrative disease. This is positive if the increase is 6 mmHg or more (20). No increase in intraocular pressure is seen in patients with non-infiltrative ophthalmopathy and in normal people (29,30). The increase in intraocular pressure is as a result of compression of the globe by a fibrotic inferior rectus muscle.

(5) Damage to optic nerve and retina.

The retina may be injured by venous congestion and haemorrhages. Optic neuropathy is a serious complication affecting about 5% of the patients (20). It occurs through direct compression of the optic nerve or its blood supply at the orbital apex by congested and enlarged recti muscle (20, 27). Papilloedema may be present and loss of visual fields is the sequel (2). As the disease progresses, pallor of the disc and decrease in central visual acuity are evident and blindness may occur. Thus compression that often occurs in absence of significant proptosis, may lead to severe but preventable visual impairment. Persistently high intraocular pressure will similarly lead to pallor and cupping of the discs. This will result in loss of visual fields and decreased visual acuity.

IV TREATMENT OF HYPERTHYROIDSM AND THE CAUSE OF GRAVES OPHTHALMOPATHY

Graves ophthalmopathy may occur before, concomitantly with but also after onset of hyperthyroidsm (5).

Thus both hyper- and hypothyroidism may account for the progression of Graves ophthamopathy. The non-infiltrative ophthalmopathy corrected by control of thyrotoxicosis, no matter which therapeutic route is used (7, 10).

The effect of treatment for hyperthyroidism on infiltrative ophthalmopathy is largely unclear.

i. Antithyroid drug treatment

Antithyroid drugs inhibit the synthesis of thyroid hormone leading to a gradual reduction in serum thyroid hormone levels (7).

Restoration of euthyroidism by thionamides has been reported to be associated with an amelioration of eye disease. Propylthiouracil treatment has been associated with progression of eye disease. The major drawback of use of antithyroid therapy is represented by a large number of recurrences after drug withdrawal or when tapered down (2).

Antithyroid drug treatments are also associated with unsatisfactory control of hyperthyroidism (31, 32).

ii. Radioiodine therapy

Radioiodine destroys thyroid follicular cells due to its ionizing effects (27). It is widely used in treatment of Graves related hyperthyroidism.

Radioiodine has been associated with progression or development of ophthalmopathy in some patients especially the smokers (33). This is due to release of thyroid antigens after

radiation injury (4). Concomitant use of prednisone for about three months prevents radioiodine-associated progression of ophthalmopathy (34).

iii. Iodine

Iodine blocks thyroid hormone release acutely. It is therefore used to prepare patients for thyroidectomy by decreasing vascularity of thyroid gland. It is also used in management of thyrotoxic storm and as an adjunct after radioiodine therapy (27).

iv. Thyroidectomy

Thyroidectomy removes the bulk of thyroid gland and hence the follicular cells thus decreasing production of thyroid hormone (27).

As with radioiodine, the issue of whether thyroidectomy affects the course of Graves ophthalmopathy is also unsettled. Thyroidectomy per se seems to carry a very low risk of causing Graves ophthalmopathy progression (2).

In contrast glucorticoid treatment is not necessary after thyroid surgery as it is in radioiodine therapy (2).

v. Total thyroid ablation

This may be achieved by a combination of both radioiodine treatment and thyroidectomy but rarely by each alone (35,36).

If Graves ophthalmopathy is well established it is conceivable that orbital auto immunity might proceed independently of the removal of thyroid tissue.

Therefore total thyroid ablation may not influence favourably the course of the eye disease (2).

V MANAGEMENT OF GRAVES OPHTHALMOPATHY

The aim of the ophthalmologist is to restore a normal pressure-volume relation within the orbit (27).

i. Management of non-severe Graves ophthalmopathy.

In mild ocular involvement simple local supportive measures will normally obtain symptomatic relief until eye disease becomes inactive. The most important thing is to reassure the patient that chance of his Graves ophthamophathy progression to severe form is low and regression is high (2).

These include: -

1. A change in sleep position and elevation of the bed will help to decrease periorbital oedema. Use of diuretics as well as decreasing salt intake is still open to debate (37).
2. Tinted glasses come in handy in case of photophobia and shielded glasses can be used to prevent eyes from irritation.

   Protective drops, 5% methylcellulose and a protective ointment at night help to relieve foreign body and gritty sensation due to a defective tear film (38).

   A 0.5 % solution of hydrocortisone can prove beneficial when used for a brief period of time as eye drops three times a day in combating some of the local irritative phenomenon. However it is associated with herpes simplex virus infection and increased intraocular pressure.
3. If lagophthalmos is present (suggested by tearing and eye irritation) taping the eyelids shut during the night is useful to prevent nocturnal corneal drying (38).
4. Guanethidine or β blocking eye drops have been used to prevent lid retraction. However long term efficacy of guanethidine is questionable. It is also associated with side effects like ptosis, miosis, vasocongestion and puntate keratitis (37).

5. Prisms are beneficial for correction of mild diplopia, with stick on prisms allowing greater flexibility than ordinary prisms (39). Diplopia can be handled temporarily by use of an eye pad or occluding one lens of the patient.

ii. Management of severe Graves Ophthalmopathy

1. Glucocorticoids

These have been used for over forty years successively (40). Glucocorticoids have both anti-inflammatory and immnosuppressive actions, including interference with function of T and B lymphocytes. They also decrease recruitment of neutrophils, monocytes & macrophages into the inflammed area and inhibit the release of mediators like cytokines (41).

In addition glucorticoids decrease glycosaminoglycan synthesis and secretion by orbital fibroblasts (42, 43).

Different routes have been used; - oral, intravenous and local (38).

(a) Oral glucocorticoid

Oral glucocorticoids are used in high doses, like prednisone 60-100mg per day and for a prolonged period of time (several months). High effectivity has been reported on soft tissue changes and optic neuropathy, where as in proptosis and improvement in ocular motility has not always been impressive (4, 38, 41). Recurrence of active disease is rather frequent problem after withdrawal or when glucorticoids are tapered down. The recurrence has been found to be abated when cyclosporine is used concomitantly with and after glucocorticorid therapy (44).

(b) Intravenous glucocorticoid

Intravenous administration of methylprednisone acetate (0.5 – 1mg) at different intervals is used (2). Favourable results have been noted on inflammatory signs and optic nerve involvement.

Intravenous steroids have been found to be slightly more effective and cause fewer side effects than oral glucorticoids. This was shown by results of a prospective single-blind randomized study 44 of 82 patients to compare the effectiveness and tolerability of Intravenous and oral steroids associated with orbital radiotherapy.

A major drawback of systemic glucorticoid therapy is represented by possible side effects and complications. These are cushingoid features, diabetes, depression, reactivation of chronic disease, hypertension, osteoporosis, weight gain, peptic ulcer, hirsutism and cataract development (38).

(c) Local (retrobulbar or subconjuctival).

Therapy by this route is considered in patients with active ophthalmopathy and with major contraindications to the systemic administration of glucorticoids (38). However the results are much less satisfactory than with systemic treatments. The side effects are limited to transient ocular discomfort or pain.

Steroids may be administered in conjuction with radiotherapy (2) and with cyclosporine (44) and appear to potentiate the efficacy of both.

2 Orbital radiotherapy

Orbital radiotherapy has been used for several decades in management of Graves ophthalmopathy (46). It should be considered as an alternative to systemic steroid therapy in patients who have contraindications to or are unresponsive to steroids. Radiotherapy has both nonspecific and anti-inflammatory effect and has high radiosensitivity to lymphocytes infiltrating the orbital space (47). A positive response is usually evident within six weeks with maximal improvement by four months (20).

Radiotherapy suppresses lymphocytes and decreases glycosaminoglycan production by orbital fibroblasts (48). Peterson et al (49), obtained favourable results in 60% of patients with active Graves ophthalmopathy treated with radiotherapy.

Marked improvement on soft tissues and optic retinopathy has been reported.

Orbital radiotherapy is well tolerated but can cause a transient exacerbation of inflammatory eye signs and symptoms, this being reduced by concomitant use of glucocorticoids (41).

Some of the side effects noted are;

i. Cataract formation (46)
ii. Radiation retinopathy is very rare (50)
iii. The possibility that the orbital radiotherapy may be carcinogenic is a major concern. However, no study has so far verified this though there is a theoretical risk (51).

Thus orbital radiotherapy if used in optimal doses is a safe procedure with limited side effects.

3. Orbital radiotherapy combined with glucocorticoids

These two can be used alone or in combination.

The inclusion of glucocorticoids prevents radiation associated transient exacerbation of eye disease. The inclusion of orbital radiotherapy on the other hand reduces the prevalence of recurrence of eye disease noted when glucocorticoids are withdrawn or when tapered down.

This combination is preferably used as a first choice in patients with active and moderate to severe thyroid eye disease if conservative is the way to go rather than decompression (52). In mild to moderate thyroid eye disease, irradiation of the orbit is indicated if eye movement is compromised (53, 54).

4. Orbital decompression

Orbital decompression aims to increase the intraorbital volume to relieve retrobulbar pressure (27). This is through removal of bony components of the orbit. It is especially very effective on proptosis (4).

Indications of orbital decompression (55, 56) are: -

i. Compressive optic neuropathy not responding to steroids
ii. Proptosis
iii. As a preliminary to extraocular muscle surgery
iv. Glucorticoid side effects
v. As a rehabilitative cosmetic surgery
vi. Exposure keratitis, severe eye lid retraction, chronic eye pain, subluxation of the globe

Various approaches to orbital decompression are: -

1. Lateral approach –The lateral wall is removed leaving the lateral orbital rim. This has limited effectiveness on proptosis (4).

2. Superior (transfrontal) approach

   The roof is removed and this approach is effective but rarely used because of complications and risks (57) associated. These are: -

   I. Intracerebral haemorrhage
   II. Damage to frontal lobe
   III. Meningitis
   IV. Sensation of pulsation behind the globes

3. Inferior (transantral) approach is still popular.

   This is done by removal of floor and medial wall (two wall decompression) achieving a 3-6mm retroreplacement of the globe (20). When serious proptosis is present the lateral wall may also be removed (three wall decompression) with a reduction of proptosis of between 6 - 10 mm being achieved (20). Associated complications are sinusitis, lower lid entropion, numb lip and high incidence of post-operative diplopia.

4. The four wall techniques is rarely needed but considered in very severe proptosis resulting in reduction of proptosis of between 10 – 11mm (20).

Orbital decompression is very effective therapeutic procedure of Graves ophthalmopathy but relies on availability of a skillful orbit surgeon. In addition patient satisfaction is high

(58, 59). However, orbital decompression does not solve the problem of preoperative diplopia and a number of patients will need extraocular muscle corrective surgery.

REHABILITATION SURGERY

This is crucial in that it not only improves the cosmetic appearance of the patient but also the function of his eyes.

(a) Extraocular muscle surgery

This is indicated when fibrosis is stable in patients with persistent diplopia and is not corrected by prisms. The disease should be inactive for four to six months prior to surgery. Surgery is carried out to recess the most restricted muscles (4,20,38).
Diplopia is difficult to correct it in all gazes and restoration of single binocular vision in primary and reading position must be considered a success.

If decompression is to be done for any reason, any muscle surgery should be deferred because retroplacement of the globe can affect ocular motility (27).
Inferior rectus is the muscle that most frequently requires corrective surgery followed by medial rectus (20) then superior rectus and rarely lateral rectus.
Treatment failure may be due to the fact that the extraocular muscles in Graves patients are taut and bleed easily. Eyelid swelling may make access to the operative field difficult.

(b) Eye lid surgery

Indications for this include (38),

i. To improve patient appearance

ii. To relieve discomfort

iii. To protect the cornea

Retraction of both upper and lower lids occurs in about 50% of patients with Graves disease and is responsible for functional and cosmetic problems (20).

Lid surgery should be postponed until the ophthamopathy has been stable and inactive for four to six months. In emergencies like exposure keratitis or corneal ulceration, tarsorrhaphy may be done. Eyelid surgery represents the last step if extra ocular muscles surgery is also required (20).

Surgical techniques for upper lid retraction include (20, 27),

i. Excision of Müller muscle
ii. Levator aponeurosis reccession
iii. Levator myotomy
iv. Temporal or permanent canthorrhapy
v. Inferior rectus recession of 4 mm is used where inferior rectus fibrosis is thought to contribute to upper lid retraction.

Recession of lid retractors and insertion of a scleral or cartilage graft as a spacer alleviates lower lid retraction.

Blepharoplasty can be performed with these procedures to remove excess fatty tissue and redundant skin from around the eyelid.

These procedures have about 90% success in achieving normal lid level but secondary surgery may be required in cases of under correction or over correction (24).

(c) Orbital Decompression

This can also be considered a form of rehabilitative surgery in cases of cosmetically unacceptable proptosis (56).

METHODOLOGY

Setting

The study was carried out at KNH, a national referral and teaching hospital.

Study design

This was a cross-sectional study on thyroid associated eye disease conducted in patients attending the thyroid clinic at KNH. The study was conducted in May and June 2004 for a period of five weeks.

Sample

A total of one hundred and eleven patients were seen at the thyroid clinic during the five weeks study period. All patients attending the thyroid clinic for that period were reviewed (by the investigator) and those who fulfilled the inclusion criteria below were entered into the study.

Inclusion criteria:

i. Known hyperthyroid patients confirmed by biochemical test
ii. New patients suspected of thyroid eye disease by clinical evaluation and later to be confirmed by TFTs (T3, T4 and TSH)
iii. Patients who were euthyroid but were on treatment for thyroid dysfunction
iv. Hypothyroid patients confirmed by biochemical test
v. Patients with goitre

Patients who did not meet the above inclusion criteria were excluded from the study.

Procedure

Patients were explained the purpose of the study and the assessment that would be performed. For those who met the inclusion criteria and obliged, an informed written consent was signed. For children below 18 years of age, the parents or guardians were asked to sign the consent form. A serial number was then assigned to each of these patients.

A detailed history and thorough physical examination was performed. Information regarding patients` age, sex, race, duration of thyroid disease, ocular complaints and its duration were recorded, drug history. History regarding presence of other systemic medical illnesses including diabetes and hypertension were noted. Surgical history involving the thyroid or the eye was inquired into and all these were entered into a questionnaire. The patients were further interviewed and the following symptoms of TAED specifically asked for:

i. Pain with or without eye movement
ii. Decreased vision
iii. Foreign body sensation in the eyes
iv. Redness of the eyes
v. Fullness behind the globe
vi. Double vision

Eye examination was then conducted for every patient. Visual acuity was assessed with a Snellens chart, each eye at a time. Those with abnormal vision were refracted to rule out refractive errors.

Extraocular motility was assessed and any extraocular muscle restriction noted. In each position of gaze, the patient was asked for presence of diplopia. Diplopia was classified as intermittent if it was present only when fatigued, inconstant when present in secondary positions of gaze and constant when present in primary position.

The patients with clinical signs of proptosis, were examined with a Hertel`s exophthalmometer and the degree of proptosis was graded as mild (20-22), moderate (23-24) or marked (>25). The palpebral fissure was measured using a ruler and was graded as mild (9-10mm), moderate (10.5-13mm) and marked (>13).

Presence of goitre or a thyroid scar was recorded.

The clinical signs of TAED were assessed by inspection of anterior segment of the eye using a torch and a portable slit lamp. The following clinical signs were looked for:

i. Lid oedema and erythema
ii. Lid lag
iii. Lid retraction
iv. Conjuctival chemosis and injection
v. Swelling of the caruncle
vi. Corneal involvement

The quantity of tear production was assessed for each eye. This was performed using the Schirmers strips and was reported as normal (over 15mm), moderately reduced (5 to10mm) or markedly reduced (less than 5mm).

Intraocular pressures were measured in primary position with a Schiotz tonometer and recorded as normal, increased or reduced. A difference of 6mmHg or more between intraocular pressures in elevation and primary position was significant and entered in the questionnaire.

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Fluorescein strips were used to stain the cornea to check for any corneal involvement. Fundoscopy was performed using monocular indirect and direct opthalmoscopes. Disc condition was observed as normal, oedematous or atrophic. Choroidal folds were specifically looked for. Visual fields were assessed, in every fifth patient, with the Humphreys automated perimeter. Visual field changes were recorded as normal, constricted and others depending on the finding. Muscle thickness was measured for every fifth patient with an ultra sound. Measurements for each of the recti muscles were recorded in millimeters.

The patients' records were reviewed and the thyroid function tests obtained. Depending on the biochemical tests, the thyroid functional status was classified as hypothyroid, euthyroid and hyperthyroid.

The clinical activity score was assessed for each eye. To achieve this, a point was awarded to each of these parameters; presence of retrobulbar pain, pain on eye movements, eyelid erythma, eyelid oedema, conjuctival injection, conjuctival chemosis and swelling of the caruncle. A score of 4 or more indicated active disease.

The severity of eye disease was assessed by the degree of proptosis, diplopia and optic neuropathy. Proptosis was measured as mild (19-20), moderate (21-23) and marked (>23), while diplopia was graded as mild if it was intermittent, moderate if it was inconstant and marked if it was constant. Optic neuropathy was assessed as mild if it was sub-clinical, moderate it visual acuity was 6/9-6/12, and marked if visual acuity was worse than 6/12. The severity of TAED was graded as severe or non-severe. TAED was

graded as severe if there was at least one marked or two moderate or one moderate and two mild parameters.

Data management

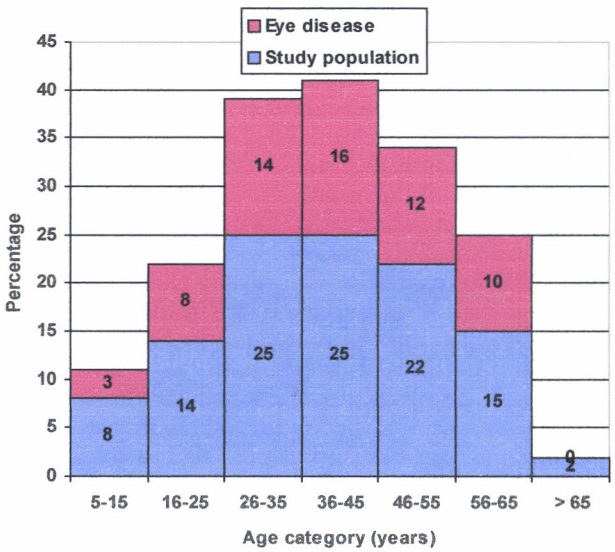
Data was entered into a questionnaire for each patient. This included information from direct questioning, clinical examination and review of medical records. This data was stored in SPSS in a personal computer awaiting analysis. Once all data was collected analysis was done using the SPSS version 10.

RESULTS

A total number of 111 patients were reviewed during the study period. 64 had thyroid associated eye disease. The results are presented below.

Figure 1: Histogram showing age distribution of study population and patients with TAED

Patients in all age groups were reviewed. They ranged between 7 and 80 years. The age was normally distributed.



2. Sex distribution of thyroid associated eye disease

103 females and 8 males were studied

F: M ratio 13:1

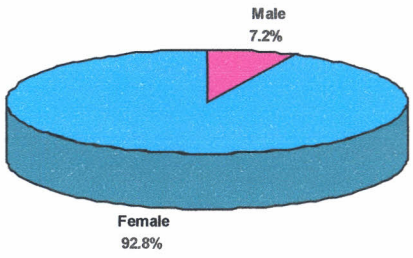


Figure 2: Pie chart showing sex distribution of TAED

3. Laterality of eye disease

Bilateral disease occurred in 62 patients. Only 2 patients had unilateral disease.

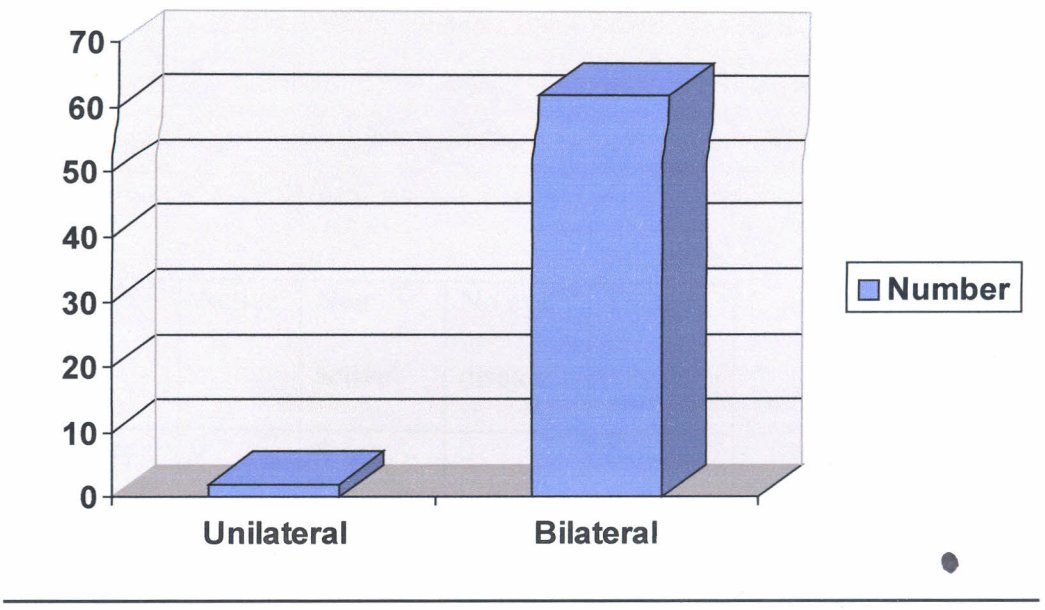


Figure 3: Bar chart showing laterality of eye disease

4. Severity and activity of TAED in study population

53 (83%) patients had non-severe disease while 11 (17%) had severe disease.

Active disease was found in12 of them.

	Active	Non active	No eye disease	Total
Severe	7	4	0	11
Non-severe	5	48	0	53
No eye disease	0	0	47	47
Total	12	52	47	111

Table 3: Severity and activity of TAED

5. Distribution of eye disease by sex.

TAED occurred in 58 females and 6 males

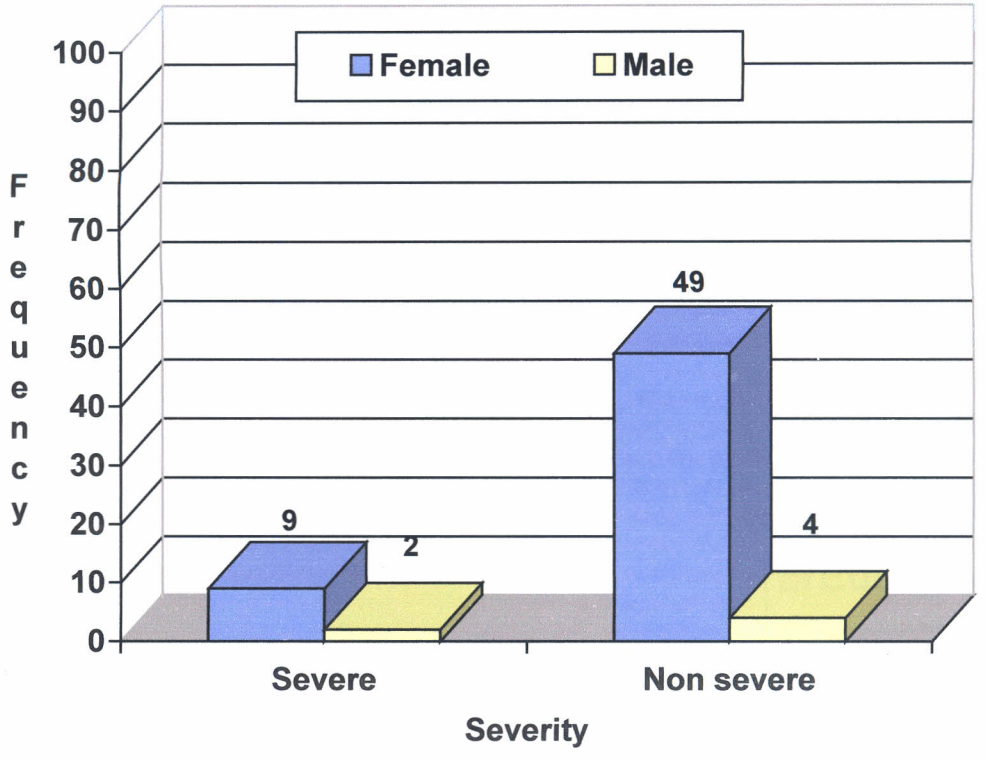


Figure 4: Bar chart showing the distribution of TAED by sex

5. Distribution of TAED by thyroid hormone levels

Patients with a hyperthyroid state had comparatively more severe disease than either euthyroid or hyperthyroid

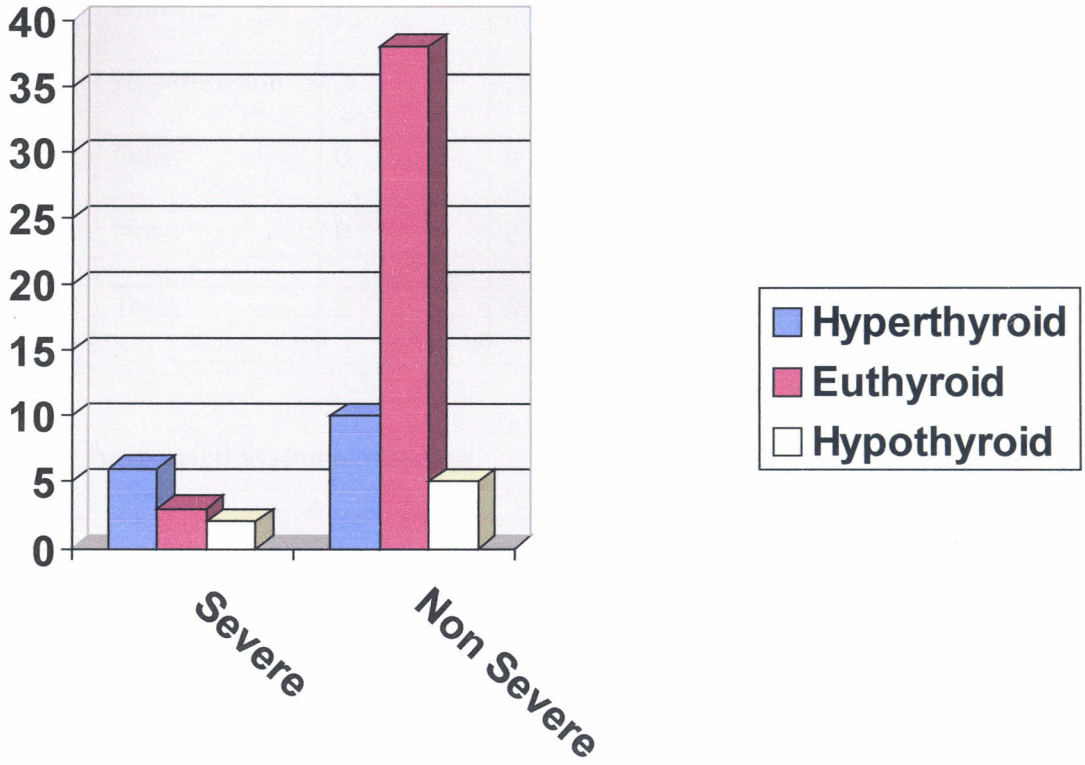


Figure 5: Bar chart showing distribution of TAED by thyroid hormone levels

7. Associated systemic diseases

Hypertension was a common finding in 47 out of 111 patients. Diabetes occurred in only 3 patients who had non-severe disease.

N=111

	Unilateral	Bilateral	No disease state	Total
Diabetes	0	3	0	3
Hypertension	2	28	17	47
Other	0	8	4	12
None	0	23	26	49
Total	2	62	47	111

Table 4: Associated systemic diseases

8. TAED occurrence in relation to duration of thyroid disease

72% (46) patients presented with ocular disease within 5 years of diagnosis of thyroid disease.

N=64

Duration since diagnosis of thyroid disease	Number of patients TAED	Percent
0-5 years	46	72
6-10 years	8	13
11-15 years	6	9
16-20 years	0	0
21-25 years	4	6
Total	64	100

Table 5: TAED occurrence in relation to duration of thyroid disease

9. Subjective correlation of when eye disease began in relation to thyroid disease

22 patients responded positively to having eye disease. 31.81% of them had ocular symptoms long before the systemic manifestations of thyroid disease. 50% had ocular symptoms after the diagnosis of thyroid disease, while 13.64% presented with ocular symptoms after the thyroid disease was controlled. 4.55 % of them had eye disease but did not know when it began.

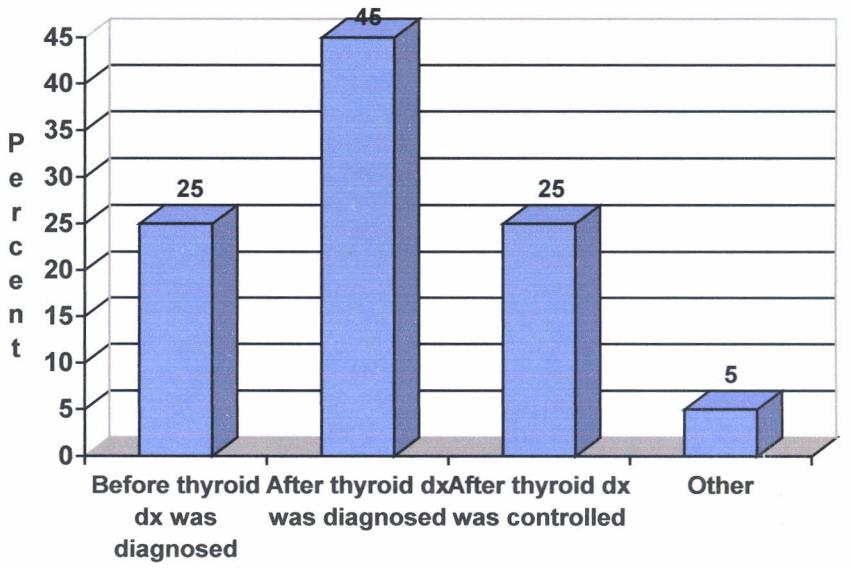


Figure 6: Bar chart showing subjective correlation of TAED occurrence in relation to thyroid disease

10. Symptoms of TAED

The commonest complaints were redness and foreign body sensation. Only 6.3% of patients complained of diplopia.

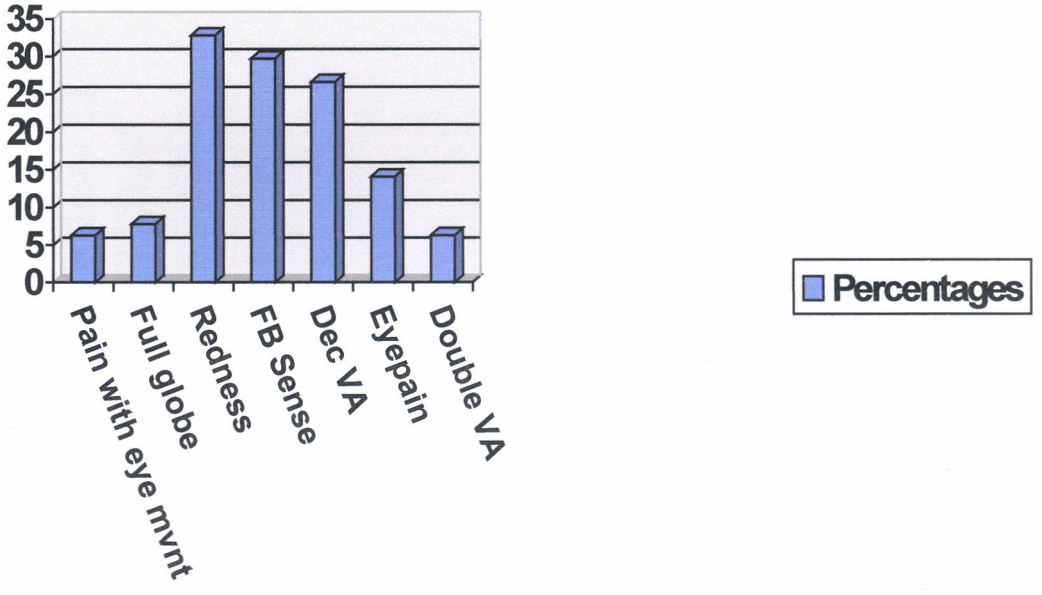


Figure 7: Bar chart showing symptoms of TAED

11. Signs of TAED

Conjuctival injection was the most frequent finding in thyroid associated eye disease. It occurred in 58% of the patients. Most of the patients had multiple signs.

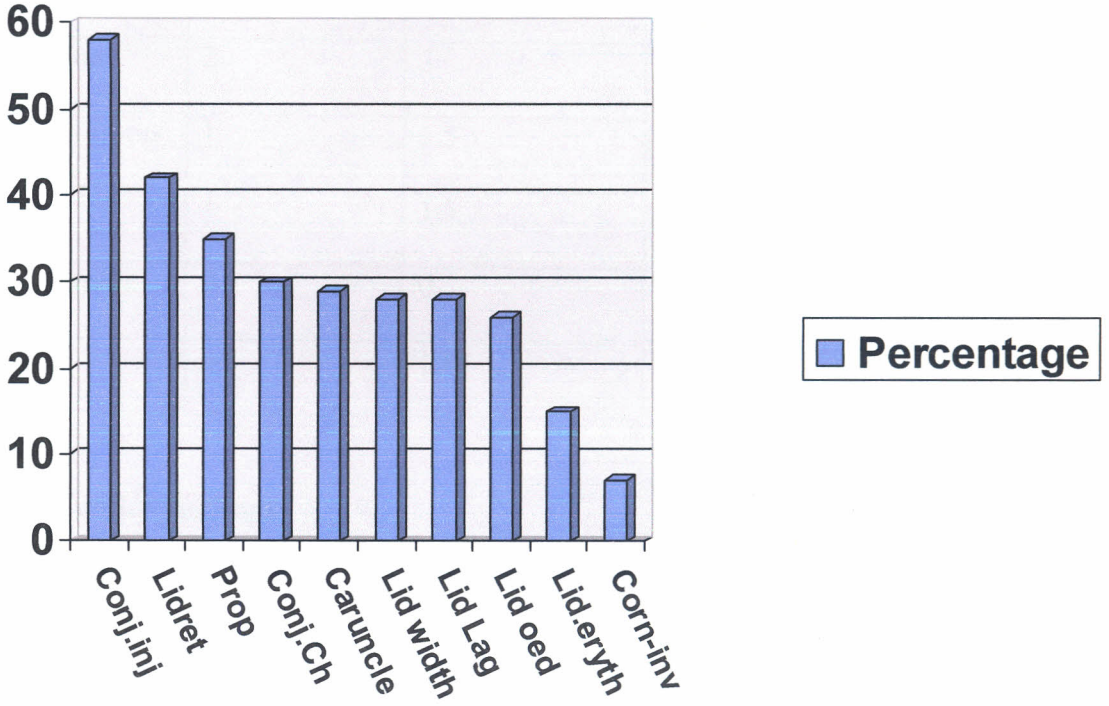


Figure 8: Signs of TAED

12. Fundus findings

N=64

Condition	Number	Percentage
Normal	52	81
Increased CDR	5	8
Pallor	3	5
Disc oedema	2	3
Myelinated fibres	1	1.5
HR	1	1.5
Choroidal folds	0	0
Total	64	100

Table 6: Fundus findings

13. Increased muscle thickness

22 (44 eyes) patients had muscle thickness measured.13 of them had enlarged muscles and 11 of them had at least one inferior rectus thickened.

N=44

Muscle	Number	Percentage
Inferior rectus	21	47.7
Medial rectus	9	20.5
Superior rectus	4	9.1
Lateral rectus	1	2.3

Table7: Increased muscle thickening

14. Complications of TAED

Diplopia

N=64

Diplopia	Number	Percentage
Intermittent	3	4.7
Inconstant	0	00
Constant	2	3.1
No diplopia	59	92.2
Total	64	100

Table 8: Diplopia

Visual field changes

N=22

Visual field change	Number	Percentage
Constriction	2	9.1
Central scotoma	2	9.1
No visual field change	18	81.8
Total	22	100

Table 9: Visual field changes

14. Treatment of thyroid dysfunction in KNH

N=111

	Patients with TAED	No TAED	Total	Percentage
Antithyroid drugs	23	6	29	26.1
Thyroidectomy	7	8	15	13.5
Combination	11	9	20	18.1
No drugs or surgery	23	24	47	42.3
Total	64	47	111	100

Table 10: Treatment of thyroid dysfunction in KNH

15. Treatment of TAED

N=64

Treatment	Number	Percentage
Steroids	16	25
Steroids, artificial tears, Teo		1.5
Steroids, artificial tears, Betoptic	1	1.5
Patching	1	1.5
Tarsorhaphy	1	1.5
Decompression	0	0
Radiotherapy	0	0
Other	2	3
None	42	66
Total	64	100

Table 11: Treatment of TAED

Distribution of thyroid patients by age and sex

Patients in all age groups and sex were reviewed.103 (93%) of them were females and only 8 (7%) were males. The female to male ratio was 13:1.This is comparable to studies that have been done where the ratio has been reported as 10:1 (8).

Although only 8 men were seen during the study, 6 (75%) of them had thyroid associated eye disease. This is much higher compared to 54% of women who had the disease. Thyroid orbitopathy like other autoimmune diseases, is known to occur more commonly in women than men. It is not known why women are affected more.

In this study all age groups were seen but as has been found in other studies, the extremes of age are less affected. Many studies point out that only 1-5% of Graves patients are less than 15 years of age (2,9,10,11). In this study, children below age 15 years constituted 4.7%% of all those who had TAED.

The 36-45 year is the commonest affected age group. It is also the age group in which Graves disease occurs commonly. Many studies agree with this (2, 9, 10, 11).

Ocular involvement

64 out of 111 patients studied had thyroid associated eye disease giving a prevalence of 58%. This is a lower prevalence compared to the previous local study that was

done in 1988. The prevalence then was reported as 76.9%. This difference may be due to patient education and awareness. This has lead to earlier diagnosis and treatment of both thyroid disease and TAED. Early diagnosis and treatment of thyroid dysfunction has been known to be associated with an amelioration of eye disease (2). Physicians are now more knowledgeable and have more tools for earlier diagnosis.

This prevalence (58 %) is slightly higher but comparable to what is reported in other studies as 25-50% (21). 62 of 64 patients with TAED had bilateral disease. This is an expected finding because thyroid disease is a systemic disease. In most of these patients, the involvement was asymmetrical.

Severity and activity of eye disease

83% of the patients with TAED had non-severe form of the disease. Many studies have shown this to be the presentation (2, 20, and 21). Only 17% of the patients had severe disease. This is comparable to other workers who found severe disease to occur in 5% of patients (2). Active disease was found in 12 (19%). Steroid therapy would be the most effective in this group of patients with both severe and active disease (20).

Duration of thyroid disease and severity of eye disease

A big proportion of patients (72%) presented with eye disease within 5 years of diagnosis of thyroid disease. In comparison, only 12.5 % and 9.4% of patients who had thyroid disease for 6-10 and 11-15 years respectively, had thyroid associated eye

disease. Recent studies have pointed out that TAED can occur long before systemic disease, with systemic disease or years after control (5). In this study, 11% of patients had ocular manifestations before systemic disease. Marcocci et al (5) reported that regardless of which occurs first, the other develops within 18 months in 85% of affected patients. Other workers have reported that occurrence of Graves disease and Graves opthalmopathy is concurrent since careful evaluation of these patients reviews ocular involvement in majority of patients (2,6).

Clinical manifestations of TAED

Extraocular muscles

Extraocular muscles were enlarged in 59 % of patients. This was demonstrated by ultra sound. As in other studies, inferior and medial recti were found to be most involved in that order (2). It is not known why these two muscles are frequently involved compared to other extraocular muscles. These muscles become infiltrated, inflamed and hypertrophy due to increase in glycosaminoglycans. (10,16,27).

In this study, muscle thickness was proportional to the amount of proptosis. After recovery from inflammation, muscles undergo fibrosis and later atrophy (20). This is what is responsible for fixed strabismus and diplopia. In this study 3% of patients were found to have diplopia in upgaze as inferior rectus was fibrotic. 8 patients were found to have extraocular muscle restriction but with no diplopia. 6 of them were noted to have increased intraocular pressure on elevation. The increase in intraocular

pressure is as a result of compression of the globe by a fibrotic inferior rectus muscle (29,30).

Muscle enlargement at the orbital apex compresses the optic nerve causing optic neuropathy (20,27). In this study, optic neuropathy was found to occur but did not relate to the level of proptosis.

Lids

Lid retraction was found to occur in 42 % of patients. This was the second commonest finding after conjuctival injection. Bartley et al (24) found lid retraction to occur in 91% of hyperthyroid patients. In this study 35 (55 %) of patients were euthyroid. Various studies (7,10), have shown that lid retraction responds positively to control of hyperthyroidism, and this may explain the smaller percentage of patients with lid retraction in this study. In most cases lid retraction was accompanied by proptosis. This proved to be a cosmetic challenge to the patients. Lid retraction is chemically induced by over action of Muller muscle. This is as a result of sympathetic over stimulation secondary to high levels of thyroid hormone (25).

Lid oedema occurred in all patients who had severe eye disease. It was uncommon in those with non-severe disease. Lid oedema is caused by infiltration of cells behind the orbital septum (20).

Proptosis

Bilateral proptosis occurred in 34 % of patients. TAED is the commonest cause of both unilateral and bilateral proptosis in adults (20,27). In this study 15 % of patients had marked proptosis (>25mm). This is caused by increase of volume of orbital contents including fatty tissue and muscles (12,13,14). The proptosis is axial (7,27) as was the case in these patients.

Marked proptosis leads to inadequate closure of the lids. This together with reduced tear production results in exposure keratitis as found in 8% of patients in this study. Decreased tear production is caused by lacrimal gland infiltration by inflammatory cells (20,27). This can be prevented by a tear supplement during the day and an ointment at night. A tarsorrhaphy will also prevent this, but it can only be done temporary if the eye has be functional. The treatment option for marked proptosis is surgical decompression (4). No patient in this study had surgical decompression. Steroids (medical decompression) have been used but are not satisfactory in reducing proptosis (4, 38, and 41).

Choroidal folds

No patient was found to have choroidal folds. Choroidal folds are due to the increased muscle thickness, retro-orbital tissue and choroidal congestion (20).

Visual field changes

18% of patients were found to have visual field changes. 9% of them had generalized constriction and the other 9% had central scotomas. The visual field changes were attributed to ischaemic optic neuropathy and glaucomatous changes. Optic neuropathy is caused by direct compression of the optic nerve or its blood supply at the apex by congested and enlarged recti muscles (20, 27). The elevated pressures were due to compression of the globe by fibrotic rectus muscles (29, 30) as found in 6 of patients in this study. No increase in intraocular pressures is seen in patients with non-infiltrative ophthalmopathy and in normal people (29, 30).

Thyroid function tests and eye disease

61% of patients with TAED were euthyroid, 28% were hyperthyroid and 11% were hypothyroids. 5 % of the euthyroid patients had severe disease compared to 30 % of hyperthyroid and 29 % of hypothyroids. Hyperthyroidism therefore has proportionately higher level of severe disease. This is what has been found in other studies (2,6). This is because hyperthyroid patients have a higher level of thyroid hormones, and therefore the antibodies are proportionately higher. Salvi et al (6) reported that about 10% of patients

with opthalmopathy did not have hyperthyroidism but majority had laboratory evidence of immune disease.

Associated systemic diseases

41 (65%) patients with TAED had other systemic diseases. Hypertension was present in 31 of them. One of these patients had hypertensive retinopathy grade two. The association of hypertension and ophthalmopathy is because both are caused in many cases by increased thyroid hormone (2). Diabetes was present in only 3 patients. None of these had diabetic retinopathy. Rheumatoid arthritis was found in one patient who also had diabetes and glaucoma.

TREATMENT

Treatment options for thyroid dysfunction

Many of the patients in this study were taking antithyroid drugs. Thyroidectomy had been performed in 32% patients. Thyroidectomy removes the bulk of thyroid gland, thereby decreasing the thyroid hormone production (27). Even after achieving euthyroid state by these two methods as seen in 61% of patients in this study, they still presented with eye disease. This is because sensitization to production of antibodies is independent of thyroid state (2). Antithyroid drug treatments are also associated with unsatisfactory control of hyperthyroidism (31, 32). TAED may occur before, concomitantly with but

also after control of hyperthyrodism, thus both hyper- and hypothyroidism may account for TAED (5).

Treatment of TAED

Most of the patients were not on any eye treatment. Many of these patients had non-severe disease that does not require any intervention. This is comparable to other studies (2, 21) in which majority of patients had mild and non-progressive ocular involvement. Bartley et al (21) found that out of 120 patients studied, 74% required no treatment or only supportive treatment. Non-severe disease tends to improve spontaneously. In this study 2 patients were on artificial tears for dry eyes.

Steroids are the main stay of treatment of severe TAED. In this study, 25 % of patients were on steroids. Many of these patients did not require steroids, which should only be reserved for the severe cases. 2 patients were on Betoptic eye drops for glaucoma therapy. One patient had tarsorrhaphy done for exposure keratopathy due to marked proptosis and eyelid retraction. Indications for eyelid surgery include relieve of discomfort and protection of the cornea (38), as was the case in this patient.

One other patient was on patching therapy for constant diplopia. Patching is a temporary option (38). Prisms would also be a benefit to him. However extraocular muscle surgery would be the most ideal as he had severe but inactive disease. Extraocular muscle surgery is indicated when fibrosis is stable in patients with persistent diplopia. The disease should be inactive for four to six months prior to surgery. Surgery is carried out to recess the most restricted muscles (4, 20, 38). No patient had had decompression done, which is a

very effective therapeutic procedure with high patient satisfaction (58, 59). This method however relies on availability of a skillful orbit surgeon. Similarly no patient was on radiotherapy. Radiotherapy if used in optimal doses, is a safe procedure with limited side effects. It should be considered as an alternative to systemic steroid therapy (46, 47, 49).

CONCLUSION

Thyroid associated eye disease is common. Its prevalence has decreased over the past one and half decades from 76.9% (Obonyos dissertation) to 58%.

Majority of the patients get non-severe form of the disease. Many of these patients have no obvious clinical findings. They are diagnosed to have eye disease by careful evaluation including examination by ocular ultrasound. The 36-45 year age group is most frequently affected.

The occurrence of eye disease is not related to the duration of thyroid disease. Most of patients will present with eye disease in the first 5 years of diagnosis of thyroid dysfunction.

TAED occurs in a patient irrespective of the thyroid state. It can occur in hypothyroids, euthyroids as well as in hyperthyroids.

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APPENDIX II

S/No. _____

DATA COLLECTION FORM

1. Age in years (1=0-10, 2=11-15, 3=16-20, 4=21-25, 5=26-30, 6=31-35, 7=36-40, 8=45-50, 9=55-60, 10=>60) Age……

2. Sex (1=Female, 2=Male)

3. Race (1=African, 2=Asian, 3=Caucasian, 4=Others (specify))

4. When did you get diagnosed to have thyroid disease (in years)?

What treatments have you used before? (1=Carbimazole, 2=propylthiuracil, 3=radioiodine, 4=Thyroxine, 5=other (specify, 6= none)

5. (i) What medications are you using currently? (1=Carbimazole, 2=propylthiuracil, 3=radioiodine, 4= Thyroxine,5=Combination, 6=other (specify), 7= none)

   (ii) What change of eye signs are you experiencing? (1=Improvement 2=Worsening, 3=No change)

7. Have you had surgery of the thyroid? (1=Yes, 2=No)
   Presence of thyroid scar (1=Yes, 2=No)

Other medical condition: (1=Diabetes, 2=Hypertension, 3=Glaucoma, 4= Combination, 5=Other (specify) 6= None)
BP……..

8. When did you notice any eye problems?
   (1=before thyroid disease was diagnosed
   2=after thyroid disease was diagnosed
   3=after thyroid disease was treated
   4=other (specify)

9 (a) Have you been on treatment for your eyes? (1=yes, 2=no)

   (b) If yes in 9(a), what treatment? (1=steroids, 2= radiotherapy, 3=decompression,4=artificial tears, 5=patching, 6=other (specify) 7=none)

10 Fill the table.
(1=yes, 2=no)

Presence of,	Condition	
	RE	LE
Eye pain		
Pain with eye movement		
Decreased Vision		
Grittiness/Foreign body sensation		
Redness		
Fullness behind globe		
Double vision		

11 Presence of goiter (1=yes, 2=no)

12 (a) Any associated lid lag? (1=yes, 2=no)

(b) Any associated lid retraction? (1=yes, 2=no)

13 Visual Acuity

Visual acuity	Right eye	Left eye
First visit		
Subsequent visit		

Is there improvement with refraction? (1=yes, 2=no)

14 (a) Fill in the table (1=mild, 2=moderate, 3=marked, 4=none)

Parameter	RE	LE
Lid oedema		
Eye lid erythma		
Conjuctival chemosis		
Conjuctival injection		
Swelling of the caruncle		
Corneal involvement		
Lid width		
proptosis		

(b) Schirmer test I (1=Normal, 2=Moderately reduced tear production, 3=Markedly reduced tear production)

15 Clinical Activity Score (CAS) (1=0-3, 2=4-7)

	RE	LE
Condition		

16 Visual Fields
Is there any noted change (1=constriction, 2=no change, 3=other (specify)

	RE	LE
Condition		

17 Intraocular pressure (1=Normal pressure, 2=Increased pressure, 3=Reduced pressure)

	RE	LE
Condition		

18 Disc condition. (1= pallor, 2=Edema, 3=normal, 4=other (specify))

	RE	LE
Condition		

19 i Presence of extraocular muscle restriction, (1=yes, 2=no)

	RE	LE
Condition		

ii If yes, which of the muscle(s) is restricted? (1=Inferior rectus, 2=Medial rectus, 3=superior rectus, 4=lateral rectus, 5=Other (Specify), 6=None)

	RE	LE
Condition		

21 Presence of diplopia (1= intermittent 2= inconstant, 3= constant, 4=none)

	RE	LE
Condition		

22 Have you had surgery of the extraocular muscles or the lids? (1=yes, 2=no)

	Observation
EOM	
LIDS	

23 Thyroid function tests (1=hypothyroid, 2=euthyroid, 3=hyperthyroid)

24 Muscle thickness (mm)

Muscle	RE	LE
Medial rectus		
Inferior rectus		
Superior rectus		
Lateral rectus		

25 Severity of eye disease (1=severe, 2=non severe, 3=no eye disease)

	RE	LE
Condition		

26 Involvement (1=Unilateral, 2=Bilateral, 3=No disease state)