Jornal of International Medical and Biological Sciences
International Peer Reviewed Open Access Journal
JIMBS
ISSN: 2362-1311 (Online)

# Role of Thyroidectomy in Management of Thyroid Eye Disease
## A prospective Clinical Study

ORIGINAL ARTICLE

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***Received**: 13 May, 2018 , **Reviewed**: 22 May,2018, **Accepted**: 8 June , 2018*

**Vol. 3, No. 06- 2018**

***Objective**: To assess the role and outcome of thyroidectomy in treatment of thyroid eye disease among group of Iraqi patients.*

***Patients and Methods:** A prospective clinical study conducted during a period of two years in two main teaching hospital in Baghdad Medical city complex. Including 52 patients with thyroid eye diseases. All patients were examined by ophthalmologist and general surgeon, before surgery. All patients who signed the informed consent were underwent thyroidectomy and followed up postoperatively for almost 6-20 months by the same ophthalmologist and general surgeon. The ophthalmopathy was considered when the patient had a clinically evident sign and the severity of ophthalmopathy was determined according to the European Group of Graves' Orbitopathy and Clinical Activity Score. At each visit the findings of ophthalmogical examination was reported and the sign and symptoms were assessed by the ophthalmologist, on the other side, the general surgeon followed up the patients with routein follow up of thyroidectomy patients. Statistical analysis performed using a statistical software.*

***Results:** Majority of the patients aged 40 years and above, and females were dominant in a ratio of 6.6 to 1. Ophthalmopathy was proved in 23 (44.2%) of the cases, (15 with mild and 8 with moderate to severe ophthalmopathy). After thyroidectomy 16 patients get improved and 7 were not and need further management, in total 3 patients with severe ophthalmopathy needed corrective eye surgery . The improvement of ophthalmopathy was relatively better in patients with initially mild than those with moderate to severe ophthalmopathy 11/15 (73.3%) and 5/8 (62.5%), respectively.*

***Conclusions:** Thyroidectomy found to be appropriate mode of treatment for patients with thyroid eye disease and can stabilize or improve both form of mild and sever ophthalmopathy in most patients.*

***Keywords: Thyroid eye disease, Hyperthyroidism, Thyroidectomy, Eye surgery***

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***Citation**:*

*Sallom AK, Hadi NA. Role of Thyroidectomy in management of Thyroid Eye Disease- A prospective Clinical Evaluation and Outcome Introduction : 2018;3(6):68–81*

## Introduction:

Thyroid eye disease, also known as Graves' eye disease is an autoimmune condition in which immune cells attack the thyroid gland which responds by secreting an excess amount of thyroid hormone (1). As a result, the thyroid gland enlarges and excess hormones increase metabolism. The hypermetabolic state is characterized by fast pulse/heartbeat, palpitations, profuse sweating, high blood pressure, irritability, fatigue, weight loss, heat intolerance, and loss of hair and alterations in hair quality. When the immune system attacks the tissues around the eyes, it causes the eye muscles or fat to expand. The eyes are particularly vulnerable to Graves' eye disease, because the autoimmune attack often targets the eye muscles and connective tissue within the eye socket. This likely occurs because these tissues contain proteins that appear similar to the immune system as those of the thyroid gland (2,3). Ocular symptoms can range from mild to severe; but only 10-20% of patients have sight threatening disease. Another tissue that can also be involved in the immune attack of Graves' eye disease is the skin of the shins. The eyes are particularly vulnerable to Graves' eye disease, because the autoimmune attack often targets the eye muscles and connective tissue within the eye socket. This likely occurs because these tissues contain proteins that appear similar to the immune system as those of the thyroid gland (2,4,5). The main signs and symptoms of thyroid eye disease (TED) begin when the tissue around the eye is attacked by the autoimmune process, and the result is inflammation and swelling, causing , redness and pain, puffiness around the eyes, bulging of the eyes, dry eye and irritation, occurring when the eyelids cannot close completely over bulging eyes. The progressive swelling may cause increased pressure inside the eye socket pressure-pain or deep headache, which worsens with eye movements decreased vision, when swollen tissues push on the optic nerve(6–8).

The etiology of TED is not well recognized, however, when the immune system attacks the muscles and other ocular tissues in the eye socket, the swelling and scarring resulting from the inflammation causes symptoms and signs noted above. In severe cases, the cornea may ulcerate, or the optic nerve may be damaged, either of which may result in a permanent loss of vision if not treated appropriately. The former is often due to a combination of the eyes bulging forward and scarring resulting in the eyelids retracting backward. The latter is due to thickened, inflamed and/or scarred muscles impinging on the optic nerve at the back of the socket (5,6). In most patients who develop thyroid ophthalmopathy, the eyes bulge forward or the eyelid retracts to some degree. Many patients with mild to moderate Graves' ophthalmopathy will experience spontaneous

improvement over the course of two to three years or will adapt to the abnormality. Severe ophthalmopathy will affect 10% of patients. It is caused by inflammation of the muscles, which causes them to swell. They can also become stiff (scarred), which interferes with movement of the eyes and causes double vision or impinges upon the optic nerve, causing loss of vision. In some patients, eye protrusion makes it difficult for the lids to close properly and the cornea becomes exposed and vulnerable (9,10). When the optic nerve is compromised, progressive and irreversible vision loss occurs. Rarely, orbital swelling may precipitate glaucoma that also affects the optic nerve. The muscles around the eye are particularly susceptible to the attack of lymphocytes as they tighten and lose their ability to stretch, these symptoms can occur the eye is pushed forward in its socket causing a "staring" appearance restriction of the eye's normal movements, resulting in double vision as symptoms build, many patients fear they will lose their vision (6,8). The epidemiological studies showed that globally, millions of population diagnosed annually with Graves' eye disease for instance, almost one million Americans are diagnosed each year(8,11) . Graves' disease is the most common cause of hyperthyroidism, accounting for 60-80% of cases, and exhibits a female predominance; women are five to eight times more likely than men to get the disease. The highest risk of onset is between 40 and 60 years of age. There is a similar prevalence among Caucasians and Asians with a lower prevalence among African- Americans(12). Cigarette smokers are at significantly increased risk to develop the disease, and when they do, often have more severe and prolonged activity that threatens vision. Although TED both stem from the immune system's attack on healthy tissue, one disease does not directly cause the other. That's why treatment of the thyroid gland, while important, does not improve the eye disease. The two diseases run their separate courses and do not necessarily occur at the same time, ophthalmopathy is known to precede or follow endocrine features of thyrotoxicosis, typically occurring within 18 months(6,13) .

As clinically evident ocular signs are present in about 50% of the patients and subclinical abnormalities can be demonstrated by CT, MRI. Approximately 15% of the patients will experience an aggravation of TED with chronic proptosis, diplopia and/or strabismus, inducing a significant alteration of life quality and psycho-social disorders. As no causative treatment is currently available, EO may benefit from medical decompression (high dose glucocorticoids, orbital radiation therapy) and orbital surgery(14)

Testing and diagnosis of TED depend on the diagnosis of thyroid disease , thyroid function must first be evaluated and treated appropriately by an internist, once the thyroid function is assessed, and even after treatment

of thyroid over activity and return to normal thyroid levels, the eye disease must be monitored as it often continues to progress. Eye involvement must be evaluated on a continuing basis by an ophthalmologist during the active phase of the disease and, if necessary, treated(2,15,16).

Although symptoms often resolve on their own, activity, scarring, and visual loss not readily apparent to the patient may otherwise go unnoticed and cause permanent changes(13,17).

Treatment for thyroid eye disease generally occurs in two phases; the first phase involves treating the active eye disease. This active period usually lasts two to three years and requires careful monitoring until stable. Treatment during the active phase of the disease focuses on preserving sight and the integrity of the cornea as well as providing treatment for double vision when it interferes with daily functioning and becomes bothersome(15,18,19).

Most patients experience relief from dry eyes by using artificial tears throughout the day and gels or ointments at night. Some patients also use eye covers at night or tape their eyes shut to keep them from becoming dry if the eyelids do not close properly. Dryness occurs because the lids are retracted and cannot blink properly, because the tear-producing glands have been affected by the autoimmune process and aren't functioning well, and/or because the forward bulging of the eyes prevents them from being completely covered by the lids. In some cases, acute swelling causing double vision or loss of vision may be treated for a limited time with prednisone(20–23). However, prednisone given for more than a few weeks at the dosages required to suppress the autoimmune inflammation always causes bothersome side-effects that may become severe. In patients who respond to prednisone, radiation therapy may be offered to reduce swelling, double vision, and, in severe cases, loss of vision. Most people get relief from their symptoms within two months of the radiation. However, radiation treatment is only marginally effective at reducing these abnormalities and may cause ocular dryness. It can only be used at most twice in a person's lifetime and bears a slight risk for inducing tumors. Surgical decompression can also be used during the active phase, most often to relieve optic neuropathy. It is also helpful in reducing congestion, redness, pain, and ocular exposure. Treatment during the remission phase that lasts indefinitely in most cases, involves correcting unacceptable permanent changes that persist after the ocular conditions of the active phase have stabilized. In the second phase, treatment of permanent changes may require surgery to correct double vision and reduce eyelid retraction. Surgery may be helpful in returning the eye to a normal position within the socket (orbital decompression). It is important to stop smoking in order to reduce the severity,

duration of activity, degree of scarring, and risk of optic nerve involvement, greatly improving the success of treating TED(5,7,24). The effect of thyroidectomy on the course of the disease, either as a mean to control thyrotoxicosis or to remove the thyroid-orbit shared antigens, still under debate (1,3,12,15,24–26), hence the present study performed to assess the effect of thyroidectomy on the ophthalmologic complications associated with thyroid eye disease among group of Iraqi patients.

## Patients and Methods:

This was a prospective study, conducted during a period of Two years; April 2015 to the end of March 2017. A total of 52 patient with thyroid eye diseases and underwent total or partial thyroidectomy were included and followed up during the study period. At the Department of Surgery in Baghdad teaching hospital and Department of ophthalmology at Gazi Al Harere Hospital for surgical Specialization in Baghdad Medical city complex. The follow up of the patients performed by specialist ophthalmologist and specialist general surgeon (The researchers). Data were collected by the researchers via full medical history and clinical examination of the patients. The ophthalmological examination performed by the ophthalmologist at the time of inclusion of the patients in the study, a total of 72 eyes were examined and all findings were reported in the data form sheet that structured for the purpose of the study. The data collection sheet consisted of four parts, these are the baseline demographic data, the ophthalmological examination findings data, the thyroid related data and follow up notes at each visit after thyroidectomy. Medical history regarding treatment of thyroid disorders was obtained and reported prior to surgery.

Also early postoperative outcome was collected. The severity of thyroid eye disease at the time of presentation and at the time of operation was assessed according to the European Group of Graves' Orbitopathy (EUGOGO) and classified into mild, moderate and severe (27).

To assess the activity level of TED, the Clinical Activity Score (CAS) was used:

At the initial visit, patients are given a CAS score of 1-7 (one point for each of the following signs or symptoms) (14,27).

- *Spontaneous pain in or around the eye in the past 4 weeks (pain without eye movement).*
- *Eye pain associated with eye movement in the past 4 weeks*
- *Swelling of the eyelids*
- *Redness of eyelids*
- *Conjunctival injection (redness of the actual eyeball)*
- *Chemosis (swelling of the eyeball)*
- *Swelling of the caruncle (the red prominence at the inner corner of the eye), patient with a score of ≥ 3 considered to*

*have active disease.*

At subsequent follow-up visits, the 3 following criteria are added for a potential CAS score of 10

- *Increase ≥ 2mm proptosis*
- *Decrease in uniocular motility in any one direction of ≥ 8°*
- *Decrease in visual acuity equivalent to 1 Snellen line.*

TED is considered "active" if the CAS ≥ 3 at the initial visit, or ≥ 4 at follow-up visits.

Thyroid Surgery performed when the medical therapy, due to patient non-compliant, allergic to treatment , no resolution and recurrence of symptoms including eye disease after a course of therapy with either anti-thyroid medications or radioiodine. Also, surgery was indicated in some patients who had an associated dominant nodule and refusal of radioiodine either because the patient wanted a rapid resolution to their symptoms, had young children or desired to get pregnant, or feared exposure to radioactivity

Total thyroidectomy was performed for all patients except 3 patients underwent subtotal thyroidectomy, operative and postoperative follow up notes were recorded. Thyroid Surgery was performed by a one surgeon at a tertiary center.

Each patient's medical file was reviewed for data collection and follow up perfumed through interview with the patients at the outpatient clinic in Baghdad teaching hospital or at the private clinic. Ophthalmological examination and follow up were performed by the ophthalmologist at the hospital or private clinic

## Results

A total of 52 patients were enrolled and followed up for a period ranged 2 to 20 months , majority, (92.1%) of the patients aged ≥ 40 years. Females were predominant, represented 86.8% of the study participants with a female to male ratio of 6.6. Almost 82% of the cases of urban residence. And almost all the patients except 3 (5.3%) underwent total thyroidectomy , (**Table 1**). The signs and symptoms related to thyroid disease of the studied group at time of presentation are shown in (**Table 2**); tachycardia and or palpitations, weight loss and eye disturbances were the more frequent accounted for 57.9%, 47.4% and 42.1%, respectively, followed by heat intolerance (36.8%), anxiety/nervousness (34.2%), sleep disturbances(28.9%), tremor (26.3%), fatigue (23.7%), menstrual changes (8.9%) out of the 45 women, and the least frequent was hair loss in one patient only, (2.6%). In (**Table 3**) the type of therapy for thyroid disease that received by the patients are demonstrated where 22 patients were on anti-thyroid alone, 27 on both anti-thyroid and B-blocker while 3 patients received B-blocker alone, moreover, 8 patients have a history of receiving radioiodine alone or after medical therapy before referral. The presenting signs and

symptoms of Ophthalmopathy are shown in (**Table 4**), however, on Ophthalmological examination, 23 patients (44.2%) showed signs of ophthalmopathy ; 15 with mild and 8 with moderate to severe Ophthalmopathy , the remaining 29 patients had no signs of Ophthalmopathy (**Figure 1**). After thyroidectomy, during the follow up period, ophthalmological examination revealed that 16 out of the 23 cases with ophthalmopathy were improved to different degrees while 7 patients did not , and needed further ophthalmological management and follow up (**Figure 2** ). The improvement of ophthalmopathy was relatively better in patients with initially mild than those with moderate to severe.

Among cases with mild Ophthalmopathy 11 (73.3%) were improved after thyroidectomy, and among 8 cases with moderate to severe, 5 (62.5%), were improved (**Table 5** ).

From other point of view, thyroid replacement therapy was given to all patients. Radioiodine needed in 6 patients for their ophthalmopathy while corrective eye surgery was needed in 3 patients (all with severe ophthalmopathy initially). Fortunately none of the patients had recurrence of hyperthyroidism or serious complications.

*Table 1. Preoperative baseline characteristics of 52 patients with TED*

| Variable | | No. of patients | % |
|---|---|---|---|
| **Age** | < 40 | 4 | 7.9% |
| | ≥ 40 | 48 | 92.1% |
| **Gender** | Male | 7 | 13.2% |
| | Female | 45 | 86.8% |
| **Residence** | Urban | 42 | 81.6% |
| | Rural | 10 | 18.4% |
| **Type of thyroidectomy** | Total | 49 | 94.7% |
| | Subtotal | 3 | 5.3% |

*Table 2. Signs and symptoms related to thyroid disease of the studied group (N = 52)*

| Sign/symptom* | No. of patients | % |
|---|---|---|
| Tachycardia/palpitations | 30 | 57.9% |
| Weight loss | 25 | 47.4% |
| Eye disturbances | 22 | 42.1% |
| Heat intolerance | 19 | 36.8% |
| Anxiety/nervousness | 18 | 34.2% |
| Sleep disturbances | 15 | 28.9% |
| Tremor | 14 | 26.3% |
| Fatigue | 12 | 23.7% |
| Menstrual changes (out of 45 women) | 4 | 8.9% |
| Hair loss | 1 | 2.6% |

*Some patients had more than one sign/symptom

*Table 3. Type of therapy received by the patients before referral (N = 52)*

| Type of Therapy | No. of patients | % |
|---|---|---|
| Antithyroid alone | 22 | 42.1% |
| Antithyroid and B-blocker | 27 | 52.6% |
| B-blocker alone | 3 | 5.3% |
| Radioiodine after medical therapy | 8 | 15.8% |

*Table 4. Presenting Ophthalmological signs and symptoms of the studied group (N = 52)*

| Signs/symptom | No. of patients | % |
|---|---|---|
| Proptosis/exophthalmos | 19 | 36.8% |
| Periorbital edema | 16 | 31.6% |
| Irritation | 16 | 31.6% |
| Lid lag | 12 | 23.7% |
| Tearing | 10 | 18.4% |
| Pain | 11 | 21.1% |
| Vision changes | 8 | 15.8% |

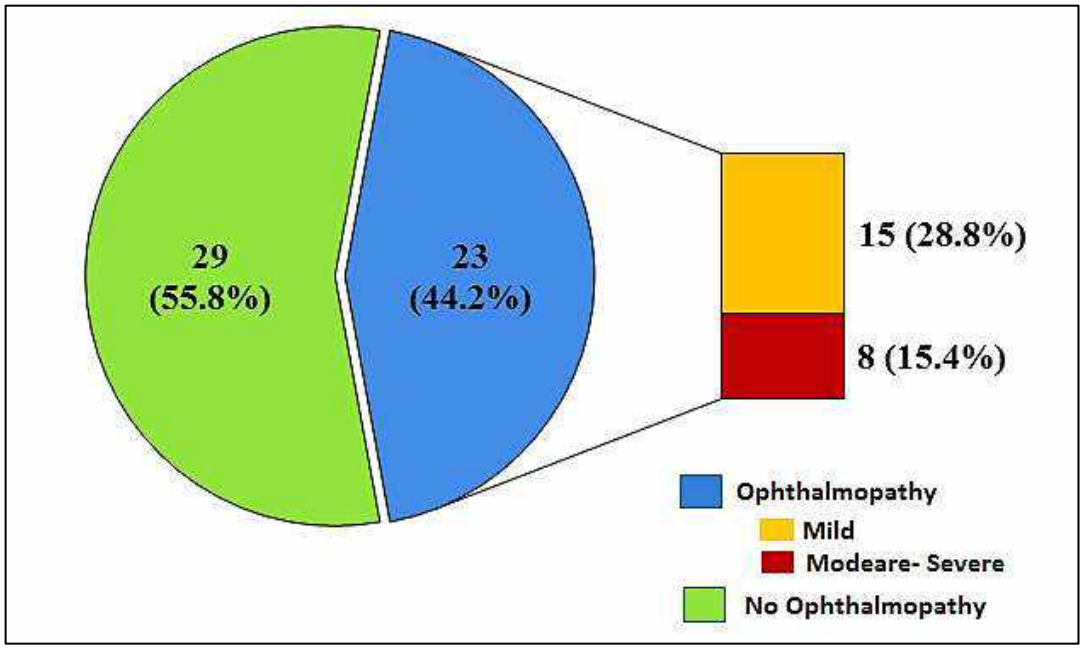


*Figure 1. Distribution of the studied group according to ophthalmological examination findings (N = 52)*

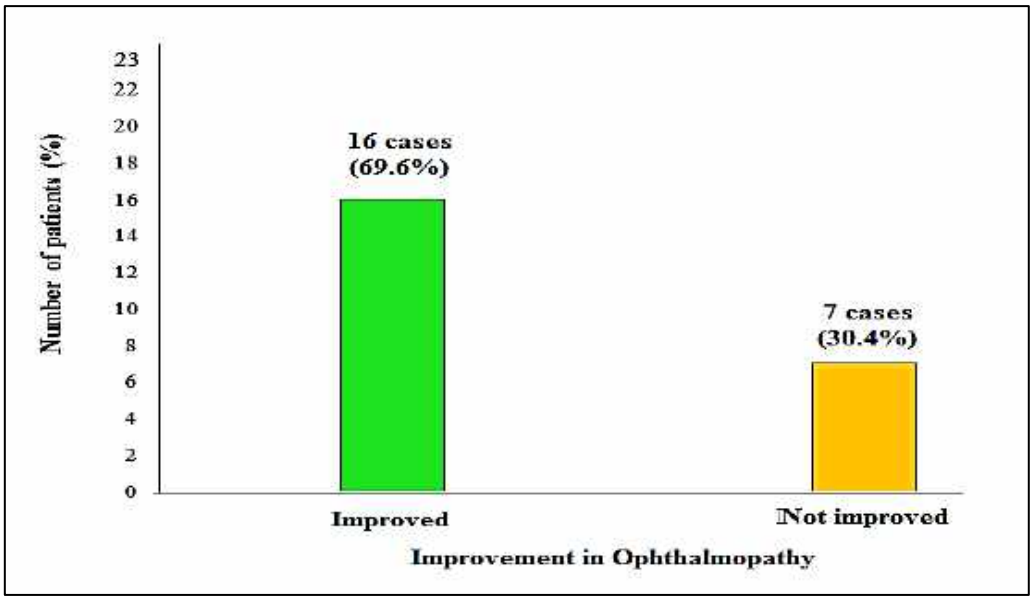


*Figure 2. Distribution of the studied group according to improvement in ophthalmopathy (N = 23)*

*Table 5. Distribution of the 23 cases with ophthalmopathy according to severity and Improvement (N = 52)*

| Ophthalmopathy | Total number of patients | Improved | | Not improved | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| **Mild** | 15 | 11 | 73.3% | 4 | 26.7% |
| **Moderate-Severe** | 8 | 5 | 62.5% | 3 | 37.5% |
| **Total** | 23 | 16 | 69.6% | 7 | 30.4% |

*Table 6. Postoperative management of the patients with TED (N = 52)*

| Postoperative | No. of patients | % |
|---|---|---|
| Thyroid replacement therapy | 52 | 100.0 |
| Radioiodine | 6 | 11.5 |
| Corrective eye surgery | 3 | 13.0 |

## Discussion

Thyroid eye disease (TED) is one of the significant health problems affecting the whole life of the patients and their families, and disturb their quality of life through its high morbidity which might end with loss of vision or other serious ophthalmic complication therefore, early diagnosis and proper management of these patients could improve their quality of life and prevent serious complication(22,23,28). There are three available forms of therapy for thyroid eye diseases, including antithyroid drugs, radioiodine and surgery . All are aim to control symptoms and to permanently reduce thyroid hormone synthesis and can improve the symptoms of thyrotoxicosis (29). However, each approach is associated with its own associated problems and failure or relapse rate. The risk for relapse has been reported to vary between 20% and 75% (26,30), nonetheless, a meta-analysis by Palit et al (31) examined 35 studies in which patients underwent total thyroidectomy or subtotal thyroidectomy for TED. No patients had persistent or recurrent hyperthyroidism after total thyroidectomy at a mean follow-up period of 5.6 years(31).

The treatment of recurrent TED can be difficult even with antithyroid drugs or radioiodine. Reoperation is certainly more difficult and carries a higher risk for complications because of the presence of scar tissue from the previous dissection (19,32). As currently, thyroidectomy can be performed with high safety by experienced surgeons, it is almost preferred for the treatment of TED, Therefore, the present study tried to assess the role of thyroidectomy in the management of patients with TED to reduce or improve their ophthalmopathy, hence a total of 52 patients were enrolled and followed up for 6 to 20 months, the follow up was made by both authors, surgeon and ophthalmologist. The present study found that majority of the patients aged ≥ 40 years and preponderance of females with a female to male ratio of 6.6 , these findings agreed that reported in epidemiological studies about TED where the incidence is higher in younger age group and females were about 5.5 to 8 folds more likely to have TED than males(8,20). In the present study, all patients received one or more type medical therapy, Antithyroid , B-blocker or combined, moreover, 8 patients received radioiodine either alone or after medical therapy, however, in all patients medical therapy failed and there was an indication for thyroidectomy. Although thyroid cancer accounts for only 1% to 2% of all cancers , its incidence is higher in TED patients , (33), however, none of our patients had thyroid

cancer. In our study, ophthalmological examination proved that 23 patients (44.2%, ) had ophthalmopathy, this reported rate was not unexpected because higher incidence of clinically evident ophthalmopathy among TED patients is widely reported. Previous two studies by Weber et al in 2006 (26) and Scerrino et al in 2012 (24) found that ophthalmopathy in almost 50% of the patients with TED and is the most common extrathyroidal manifestation of Graves' disease. The prognosis and course of ophthalmopathy are mainly affected by the choice of therapy; Tallstedt et al found that subtotal thyroidectomy and antithyroid drugs have no significant role in management of TED (34), while other studies found that ophthalmopathy could be exacerbated by radioiodine therapy, interestingly, Bartalena et al (21) reported that approximately 15% of cases who received radioiodine developed ophthalmopathy or had worsen their eye disease. Conversely, other studies proved that total thyroidectomy can improve existing ophthalmopathy (35). In the present study, 23 patients (44.2%) had different degrees of ophthalmopathy, 16 (69.6%) of them improved after total thyroidectomy , this finding supported by the fact that an increase in thyroid-stimulating hormone–receptor antibody levels was seen after radioiodine treatment, but not after medical therapy or surgery (29).

The development or progression of ophthalmopathy after radioiodine may be caused by the release of these thyroid autoantigens. The increase in anti- body production may be secondary to a lack of immune restraint caused by the effects of intrathyroidal irradiation on regulatory T cells and may account for the unfavorable response of eye involvement to radioiodine (18). Furthermore, most specialist endocrinologists agreed that thyroidectomy is useful and indicated in TED particularly in the presence of a large symptomatic goiter, and failure of medical treatment or fear of radiotherapy or the need to rapid reversal of hyperthyroidism as in pregnancy. Our findings also revealed that thyroidectomy can improve or at least stabilize ophthalmopathy in patients with TED.

## Conclusions

Thyroidectomy found to be appropriate mode of treatment for patients with thyroid eye disease and can stabilize or improve both form of mild and sever ophthalmopathy in most patients.

**Acknowledgment:**

Authors would like to thank all patients who participated in the study, hopping they will have better life. Also we pleased to thank our colleagues of medical and paramedical staff in both hospitals where the study performed, particularly in the ophthalmology and general surgery department for their help and support.

**Ethical Issues:**

This study was Ethically approved by both department of ophthalmology and General surgery . Informed signed written consent obtained from each patient before he/she being participated.

**Conflict of Interest** : None

**Funding**: The study funded by the authors. And all investigations were made in the hospital free of charge, the patients did not bear any cost.

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