ORIGINAL ARTICLE

Eye manifestations in Iraqi patients with Graves' disease

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ABSTRACT

Background: To find the eye manifestations in patients with Graves' disease in Al-Diwaniya teaching hospital in terms of incidence and severity.

Method: In this descriptive cross-section study, we recruited 64 patients (46 female and 18 male) from November 2016 to December 2019. A complete ocular examination was done, including visual acuity and intraocular pressure measurement, ocular motility examination, slit-lamp examination, and fundoscopy.

Results: In this study, 64 patients were diagnosed with Graves' thyroid disease. The mean age of the patients was 36.87 ± 17 years (range, 19–54), the mean duration of symptoms of systemic disease was 3.2 ± 1.6 years (range, 9 months to 9 years), the mean VA test score was 0.9 ± 0.23, and elevated eyelid (retraction) was noticed in 66.1% of patients (in both eyes in 91.2% of cases). The most common complaint of the patients was foreign body sensation (61% of patients). The mean Werner's NOSPECS classification score in our study was 3 ± 2.1; the score was affected by the gender of the patients (3.41 in males vs. 2.72 in females; $p < 0.01$) and positively correlated with patient age ($r = 0.287$, $p = 0.017$).

Conclusion: Ophthalmic manifestations were common in Graves' disease, and it was positively correlated with the severity of the disease.

Keywords: Graves' disease, hyperthyroidism, thyroid-related orbitopathy.

INTRODUCTION

Thyroid eye disease is considered a part of the Graves triad, which consists of hyperthyroidism, swelling around orbits with eye manifestations [e.g., lid lag, eyelid elevation (retraction), exophthalmos, muscle restriction, and optic nerve compression], and exposure keratopathy and chemosis [1].

Nearly half of patients with Graves' disease will develop eye manifestations, and these are severe in 5% of cases. The onset of eye manifestations is usually concomitant with the onset of hyperthyroidism, but might also precede or fellow it [2].

Like most autoimmune diseases, Graves' disease affects females more than males; females are six times more affected (86% F, 14% M), and in the severe form of the disease, the female to male ratio is 4:1[3]. The rate of incidence has been reported as 17 and 2.8 cases per 100,000 of population per year for females and males, respectively; the peak incidence rate is bimodal, occur in 40–44 and 60–62-year-old females and 45–49 and 64–67-year-old males [4].

The eye findings in Graves' disease had been observed for more than a century, but there is controversy about its pathogenesis and management [5-7].

Regarding Graves disease's pathophysiology, interaction occurs between fibroblasts and thymocytes. This leads to the activation of tissue proliferation and the production of cytokines, and the activated fibroblast will produce glycosaminoglycans, ultimately leading to orbital tissue expansion [8]. The extraocular muscle becomes separated by accumulated glycosaminoglycans resulting in exophthalmos and optic nerve compression. Also, it remains fibrotic, leading to a restriction in eye movement [9].

Many treatment modalities are now available for Graves' orbitopathy, such as systemic steroids, radiation, microsurgical decompression, and immune-suppressive drugs. Also, teardrops are considered the mainstay for the treatment of mild-moderate cases.

This study evaluates the prevalence and severity of eye manifestations in patients with Graves' orbitopathy in Iraqi patients and how this correlates with factors such as age, gender, and thyroid state.

METHOD

This was a descriptive cross-section study. Sixty-four patients were enrolled from November 2016 to December 2019. All patients with a confirmed diagnosis of Graves' disease and having eye findings or complaints were enrolled in this research.

The patients' diagnoses with Graves' disease depend on clinical and laboratory findings, such as enlarged thyroid gland T3, T4, and TSH levels. Subjects diagnosed with Graves' disease were sent to the ophthalmic department at Al-Diwaniya teaching hospital for an eye exam; a comprehensive ophthalmic examination was done for every patient by the consultant ophthalmologist, including Snellen visual acuity, external eye examination, slit-lamp examination using Haag Streit set with tear film status, ocular motility exam, exophthalmometry, intraocular pressure (IOP), and fundoscopy.

The Snellen chart was used to document the vision of the patients, and a visual field test done for cases with suspicious optic nerve dysfunction. IOP was measured in the primary and up gaze position using an applanation tonometer. An ocular motility test was also done, and restriction was quantitatively recorded in scores from -1 to -4. Tear status was examined by the Schirmer test, and tear film break-up seconds were recorded as abnormal. Lid retraction was defined by exposed superior sclera in the primary position of the gaze. The degree of exophthalmos was measured using a Hertel exophthalmometer, defined as measurement > 20 mm from outer orbit bone or discrepancy more than 2 mm between both eyes. Fundus

examination was also done for the optic nerve evaluation, and neuroimaging was done when needed.

The classification of Graves' orbitopathy was based on Werner classification [10] from the American Thyroid Association (Table 1).

Ethical issue: The study was approved by the ethical committee of Al-Qadisiyah University, College of Medicine. Informed consent was taken from all patients.

RESULTS

Sixty-four patients with Graves' disease were enrolled in the study (46 F, 18 M), the mean patient age was 35.87 ± 12 years (range, 19 to 61 years), and the mean duration of symptoms was 3.2 ± 1.6 years. Most of the patients had hyperthyroidism at the time of the first visit (87.1%), but 4.2% had hypothyroid status, and the remaining were euthyroid.

Most of the patients complained of a foreign body sensation (58%) and swollen eyelids (52%) (Fig. 1). The most common recorded sign was increased IOP (79.2%), which was considered clinically significant (≥ 5 mmHg) in 15.1% of cases. The mean IOP in the straight position was 16.1 ± 2.6 mm Hg, and was increased in the up gaze to 19.1 ± 4.2 mmHg ($p < 0.001$).

Lid elevation (retraction) was detected in 62.1% of cases (Fig. 2), and affected both eyes in 89.9% of cases. Proptosis was detected in 48% of cases, and of these, it affected both eyes in 92.1%. Interjunction around the intersection of the horizontal recti was done in 39.6% of cases. Its more around medial rectus interjunction, limited ocular motility was observed in 22.3% of cases, and it is most common is up gaze followed by downgaze.

The elevated IOP in the up gaze was correlated with extraocular muscle limitation of movement. 5.1 mm Mercury opposite to 2.75 mm Mercury in the presence and absence of gaze limitation, respectively ($p = 0.03$).

The tear break up time (TBUT) test had a mean of 10.78 ± 4.32 s (range, 3–19 s), and was abnormal in 59.2%. The Schirmer test result was low in 15.7% of subjects.

The mean Werner NOSPECS classification score was 3 ± 2.1 (Fig. 2). It was highly affected by gender; higher in males than females (3.72 vs. 2.46) ($p < 0.01$) and significantly affected by patient age ($r = 0.287$, $p = 0.016$).

Table (1) Modified Werner NOSPECS classification score

score	Findings
0	No signs or symptoms
1	Only signs
2	Soft tissue involvement with symptoms and signs
3	Proptosis >20 mm
4	Extra ocular muscles involvement
5	Corneal involvement
6	Sight loss (visual acuity <0.67)

Fig (1) common complains of the patients

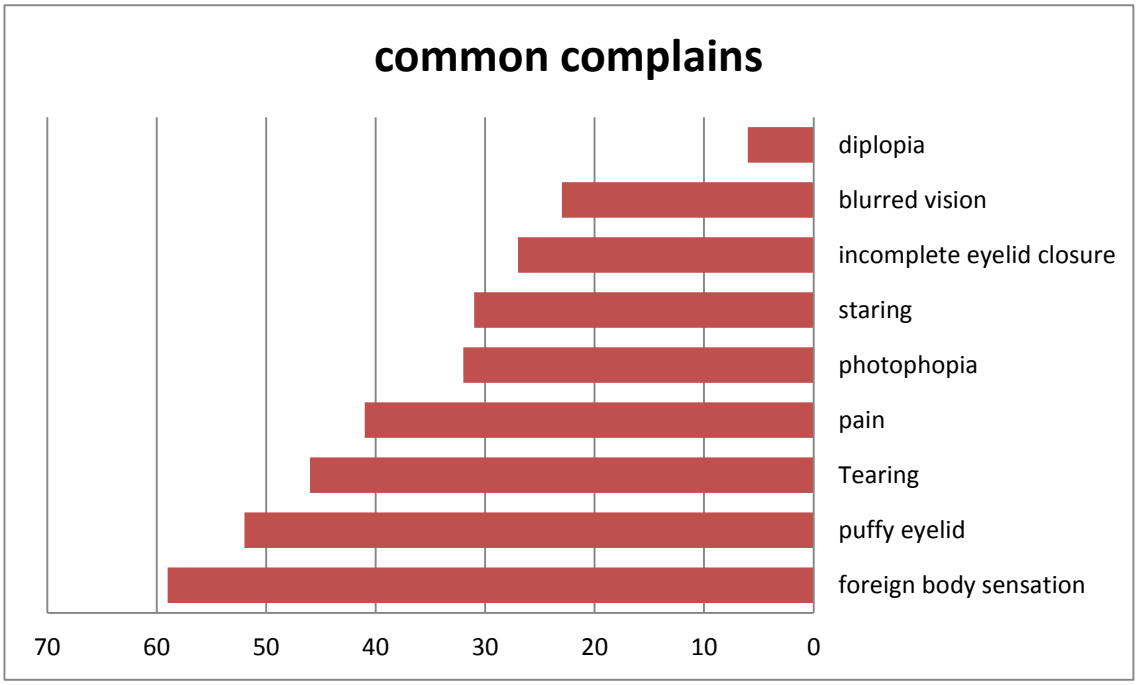

Fig (2) common physical findings

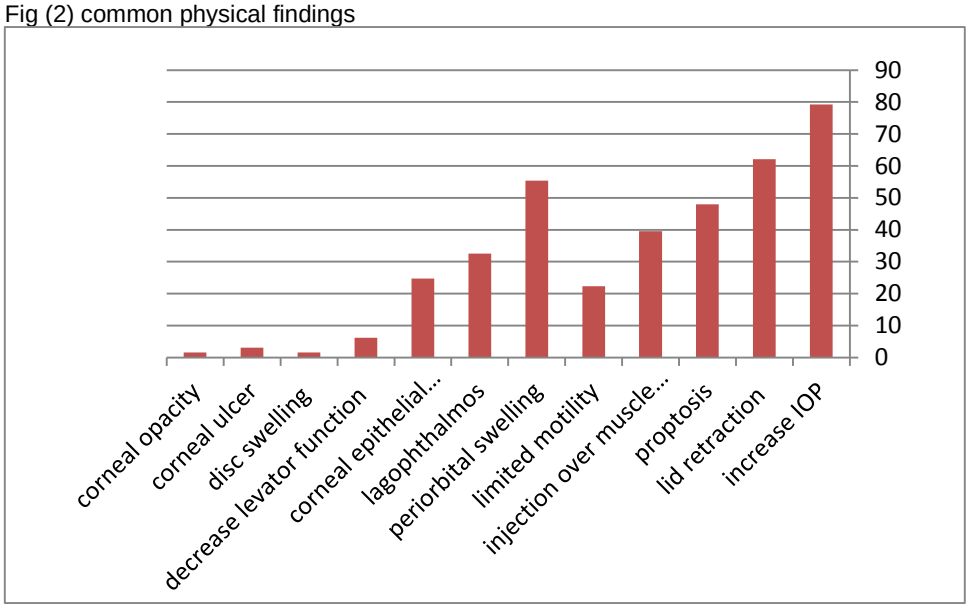

Fig (3) NOSPCS classification score, Werner score of 3 is more common

DISCUSSION

Graves' orbitopathy is an autoimmune disease, usually associated with hyperthyroidism [11]. Many studies have addressed the prevalence and incidence of thyroid-associated eye disorders, known as Graves orbitopathy; most of these studies show a female to male ratio of 4–6 to 1 [4,12,13], whereas we report a ratio of 3:1. On average, the presentation was earlier (by about 10 years) for females than males since most of the affected persons one young or middle age female, so the cosmetic issue is important.

The most common reported ocular sign was an increase in IOP (79.2%), with lid retraction present in 62.1% of cases, and proptosis in 48% of cases. These signs were of lower rates than observed in other studies: Vanghheluwe et al. [14] and Teshome and Seyoum [15].

Visual acuity was also examined using the Snellen Chart. The best-corrected VA was shown to be decreased in our study population, and the decrease was greater with advancing age [16-17], visual acuity was tested in our community population in previous studies [18, 19] and the results comparing to those with thyroid eye disease was much better, usually patient in higher age group show lower visual acuity result which might be due to other factors like cataract or nuclear sclerosis.

In our study, limitation of ocular motility was detected in 22.3% of cases, which is much lower than observed in other studies [11, 14]. Frank Strabismus observed in only 9.5% of cases in form of exotropia in most of cases.

Optic neuropathy was not observed in our study population. However, Salvi et al. used visual evoked potential to detect subclinical optic neuropathy, which had

an increased incidence after using the sophisticated technique [20]. In our study, the diagnosis of optic neuropathy was made clinically, so much fewer, more sensitive methods will be needed in future studies. Increased IOP is a common finding sit more common in up gaze. The result is similar to what find in the Gumblin study [21] elevated IOP in up gaze is significantly correlated with extraocular muscle restriction.

In our study, age and gender affect the severity of symptoms. Perros et al. [12] reported that the severity score was significantly higher in males than females and increased with advancing age.

The effect of treatment was not analyzed in this study. Additional, sophisticated research is now needed to show the effect of treatment on ocular findings and its severity.

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