



## **HYPERTHYROIDISM**

# Risk factors for developing eye disease in patients with Graves' hyperthyroidism

### **BACKGROUND**

Graves' disease is the most common cause of hyperthyroidism. Approximately 25% of patients who develop Graves' hyperthyroidism will also have clinically apparent thyroid eye disease. While thyroid eye disease is most often seen in patients with Graves' disease, it also can be seen with Hashimoto's thyroiditis and includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision. Most patients with thyroid eye disease have mild cases; severe cases can be very disfiguring and disabling and there are limited treatment options. Several prior smaller studies have reported that smoking, older age, male gender, exposure to radioactive iodine treatment, and hypothyroidism are predisposing factors for Graves' eye disease. The reason for these associations is not known. The aim of this study is to evaluate risk factors for developing eye disease in a large multicenter study of patients with Graves' hyperthyroidism.

### **THE FULL ARTICLE TITLE**

Khong JJ et al. Risk factors for Graves' Orbitopathy; the Australian Thyroid-associated Orbitopathy Research (ATOR) Study. *J Clin Endocrinol Metab.* April 7, 2016 [Epub ahead of print].

### **SUMMARY OF THE STUDY**

A total of 1042 patients with history of Graves' disease were recruited from endocrine and ophthalmology clinics in Southern Australia between 2009 and 2013. The patients' age, gender, duration since the onset of Graves' hyperthyroidism as well as eye disease, family history of Graves' disease, ethnicity and smoking status were recorded at the time of the study participation. Prior treatment for hyperthyroidism, including antithyroid medications, radioactive iodine and thyroid surgery, was recorded. The eye disease was diagnosed based on presence of symptoms and signs such as stare, red eyes, lid swelling, eye protrusion and blurred vision. An ophthalmologist performed an eye exam in all patients to assess for presence of eye disease and its severity. Several eye and vision parameters were measured, including visual acuity, inflammatory score, lid retraction and eye protrusion.

Among the study patients, 604 (58%) had Graves' eye disease (cases), while 438 patients did not have eye disease (controls). The proportion of women to men was similar in both cases and controls (4:1). The mean age of onset of Graves' hyperthyroidism was about 2.5 years later (43 years vs. 40.6 years) and the mean duration of Graves' hyperthyroidism was longer by almost 4 years (8.8 years vs. 5.0 years) in patients with eye disease as compared to those without eye disease. For every 10-year increase in age at diagnosis of Graves' disease, the risk for eye disease increased by 17% and for each 1-year increase in Graves' disease duration, the risk for eye disease increased by 7%.

The mean age at diagnosis of Graves' eye disease was 45 years. Only 4.8% of patients had onset of eye disease prior to the diagnosis of Graves' hyperthyroidism and most patients were diagnosed with eye disease within the same year as the diagnosis of Graves' hyperthyroidism. A higher proportion of cases were Caucasians (80% vs. 65%) and smokers (current and ex-smokers) (59% vs. 37%) as compared to controls. The risk of having Graves' eye disease was two times higher in smokers, as compared with non-smokers. The presence of a family history of Graves' disease and of serum TSH receptor antibodies did not differ between cases and controls.

A greater proportion of cases than controls underwent treatment for Graves' hyperthyroidism with radioactive iodine (31% vs. 16%) and thyroid surgery (23% vs. 5%), while a lesser proportion of cases used antithyroid medications (87% vs. 99%). The risk of Graves' eye disease was 7 times lower in patients treated with antithyroid medications than those not receiving antithyroid treatment.

Among the patients with Graves' eye disease, 51 (8%) developed impairment of the optic nerve function. These patients had more advanced age (mean age of 55 years) with more severe eye inflammation and restricted extraocular muscle movement. Smoking was not a risk factor for optic nerve involvement.

**HYPERTHYROIDISM**, continued**WHAT ARE THE IMPLICATIONS OF THIS STUDY?**

Older age at onset and longer duration of Graves' hyperthyroidism as well as smoking were associated with a higher risk of developing Graves' eye disease. This study confirms the predisposing factors for Graves' eye disease reported by prior studies, with the exception of male gender, which was not a risk factor in this study. Importantly, smoking is a modifiable risk factor consistently associated with Graves' eye disease in all studies.

Patients with Graves' disease should be counseled not to smoke.

— Alina Gavrilă, MD, MMSC

**ATA THYROID BROCHURE LINKS**

Hyperthyroidism: <http://www.thyroid.org/hyperthyroidism/>

Graves' Disease: <http://www.thyroid.org/graves-disease/>

**ABBREVIATIONS & DEFINITIONS**

**Hyperthyroidism:** a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid medications, radioactive iodine or surgery.

**Graves' disease:** the most common cause of hyperthyroidism. It is an autoimmune disease caused by antibodies that attack the thyroid and turn it on.

**Thyroid eye disease:** also known as Graves' ophthalmopathy. It is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis and includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

**Antithyroid medications:** block the thyroid from making thyroid hormone. Methimazole, carbimazole and propylthiouracil are used to treat hyperthyroidism, especially when it is caused by Graves' disease.

**Radioactive iodine (RAI) treatment:** iodine-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid.

**TSR receptor antibodies:** antibodies often present in the serum of patients with Graves' disease that are directed against the TSH receptor located on the thyroid cell surface, often causing stimulation of this receptor with resulting hyperthyroidism.