

## Review Article

# The hypothyroid eye

Sanjay Kalra<sup>1</sup>, Rishi Raj Singh<sup>2</sup>

Thyroid disorders are characterized by various ocular abnormalities. Though these associations are usually discussed in the context of Graves' disease, they are equally strong with hypothyroidism. This review describes the various ophthalmic disorders and complications that may occur in association with hypothyroidism. It highlights the 'thyrovigilance' that ophthalmologists and optometrists must practice while managing persons with eye disease. It also reinforces the high index of suspicion that endocrinologists and physicians should keep for conditions such as dry eye, open angle glaucoma and age related macular degeneration, while treating hypothyroidism.

[J Indian Med Assoc 2018; 116: 32-4]

**Key words :** Age related macular degeneration, dry eye, Hashimoto's thyroiditis, open angle glaucoma, ophthalmopathy.

In medicine, the term 'thyroid ophthalmopathy' suggests a correlation of eye disease with hyperthyroidism, specifically Graves' disease<sup>1</sup>. This focus, though clinically justified, may lead to neglect of eye related symptoms, signs and diseases that are associated with hypothyroidism. This brief communication reviews the various aspects of the hypothyroid eye.

### Animal Studies :

Animal and embryological studies point towards the link between thyroid health and eye development. Thyroid hormone deficiency in the developing rat is known to disrupt eye neurodevelopment. A reduction in eye volume, optic nerve cross sectional area, retinal layer thickness, and delay in glial development and myelination is observed in thyroid hormone deficient rats<sup>2</sup>. Hypothyroidism has been shown to increase oxidative stress in experimental rat models of endotoxin induced uveitis<sup>3</sup>.

Other animal studies, however, reach different conclusions. Experimentally induced hypothyroidism has been shown to have minimal, if any effect, on Schirmer tear test, intra ocular pressure, and histological parameters of conjunctival, global and adnexal tissue<sup>4</sup>.

### Peri-ocular Tissues :

The peri-ocular manifestations of hypothyroidism have been known for decades. Hypothyroidism is characterized by peri-orbital puffiness caused by deposition of hydrophilic muco polysaccharides on the dermis and other tissues. Loss of the temporal third of eyebrow may occur, but is not pathognomic of hypothyroidism. Chemosis and blepharoptosis may also be seen<sup>5</sup>.

- Ocular abnormalities are strongly associated with hypothyroidism not only Graves' disease.
- This implies a need to suspect thyroid disorders in eye related symptoms and ophthalmic complications in hypothyroidism.
- The concept of thyrovigilance should be practiced by ophthalmologists and optometrists.
- Endocrinologists and physicians must maintain a high level of clinical suspicion for ophthalmic disorders.

### Anterior Eye Segment :

The skin of persons with uncontrolled hypothyroidism may have a yellowish tinge due to hypercarotenemia. This can be differentiated from jaundice by the absence of scleral icterus in hypothyroidism. Anaemia is common in hypothyroidism, and be noted as conjunctival pallor.

Dry eye is an ophthalmic syndrome that is commonly encountered in hypothyroidism. This may be associated with proptosis. Increased palpebral tissue width may predispose to drying of the ocular surface and hyperosmolarity of the tear film<sup>6</sup>. Thyroxin receptors alpha and beta are present in the cornea, and this may explain the relation of hypothyroidism with corneal topographic fluctuations, and with keratoconus<sup>7-9</sup>. In pregnancy, hypothyroidism has been reported to cause keratoconus progression with development of acute corneal hydrops<sup>10</sup>.

The association of open angle glaucoma with hypothyroidism has been the subject of many large trials<sup>11</sup>. The Blue Mountains Eye Study<sup>12</sup> reported a significantly greater risk of open angle glaucoma in subjects reporting current thyroxin use (6.8% versus 2.8%, multivariate odds ratio 2.1; 95% confidence interval 1.0-4.4) and those with history of thyroid surgery (6.5% versus 2.8%, multivariate OR 2.5; 95% confidence interval (1.0-6.2). A five year follow up study from Taiwan has revealed similar results<sup>13</sup>.

<sup>1</sup>Department of Endocrinology, Bharti Hospital, Karnal 132001

<sup>2</sup>Department of Ophthalmology, Cygnus Hospital, Karnal 132001

### *Thyroid Ophthalmopathy :*

Severe thyroid eye disease is not always due to hypothyroidism. Primary hypothyroidism can also present with ophthalmopathy and dermopathy<sup>14,15</sup>. Auto immune disease such as systemic lupus erythematosus have a wide spectrum of clinical presentation. This may include hypothyroidism and eye involvement (uveitis and iridocyclitis)<sup>16</sup>.

Hypothyroidism following radioactive iodine ablation may continue to present with ophthalmopathy<sup>17</sup>. Eye disease may be exacerbated after radio iodine administration, due to release of orbitotropic antigens by radiation induced thyroid damage. Another mechanism is the sudden secretion of TSH which induces proliferation in retro orbital preadipocytes<sup>18</sup>.

### *Posterior Eye Segment :*

Hypothyroidism may also be associated with age related macular degeneration (AMD). A population based sample of 9677 American adults >50 years, was taken from the 2008 National Health Interview Survey. The association between AMD and hypothyroidism was significant after adjusting for all confounders (OR 1.59, 95 % CI 1.10-2.30)<sup>19</sup>.

Idiopathic intracranial hypertension may follow thyroxin supplementation for the management of hypothyroidism. Therefore, a finding of papilledema must prompt a screening for hypothyroidism<sup>20</sup>.

### *Congenital Syndromes :*

Down's syndrome is a common syndrome which presents with characteristic ocular abnormalities and hypothyroidism. Eye signs include nystagmus, esotropia, epiphora, Brushfield spots, and lens opacities, abnormalities of the retinal vessels, foveal hypoplasia, optic disc pallor, and refractive errors<sup>21</sup>.

Sturge-Weber syndrome, a rare congenital syndrome, characterized by facial port wine birthmark, can present with central hypothyroidism and eye anomalies<sup>22</sup>. The Vogt Koyanagi Harada syndrome is another example of an association between hypothyroidism and eye disease (poliosis, anterioruveitis, and retinitis)<sup>23</sup>. Peters plus syndrome<sup>24</sup>, a combination of Peters anomaly of the eye and extra ocular defects, may include hypothyroidism. This is thought to be inherited in an autosomal recessive manner.

GAPO syndrome (growth retardation, alopecia, pseudoanodontia, optic atrophy), a rare autosomal recessive disorder, may present with bilateral interstitial keratitis and hypothyroidism<sup>25</sup>. Another reported syndrome is orbital 'pseudotumour', posterior scleritis and anterior uveitis, in association with hypothyroidism<sup>26</sup>. Reported infrequently, this nonspecific orbital inflammation represents a major clinical challenge, and may be autoimmune in nature.

Jacobsen syndrome is a genetic syndrome caused by deletion 11(q23 q25). It presents with eye features such as telecanthus, downward slanting palpebral tissues, bilateral inferior colobomas (of the iris, choroid and retina) as well as central hypothyroidism<sup>27</sup>. PHACE (posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of aorta and cardio defects, and eye abnormalities) syndrome is another syndrome in which hypothyroidism coexists with eye disease<sup>28</sup>.

Congenital hypothyroidism and congenital glaucoma may coexist with other abnormalities including neonatal diabetes mellitus, in a syndrome caused by GLIS3 mutation<sup>29</sup>.

### *Summary :*

The afore-mentioned ophthalmic conditions and syndromes suggest a strong association between hypothyroidism and the eye. This implies a need to suspect thyroid disorders in persons with eye related symptoms, and to screen for possible ophthalmic complications in persons with hypothyroidism. The concept of thyrovigilance should be practiced by ophthalmologists and optometrists, while endocrinologists and physicians must maintain a high level of clinical suspicion for ophthalmic disorders.

All individual with hypothyroidism must be asked about photophobia, eye irritation, diplopia or a change in usual acuity (Singer, 1995). Similarly, all persons presenting with these symptoms must be screened for hypothyroidism.

### REFERENCES

- 1 Kumari R, Saha BC — Advances in the management of thyroid eye diseases: An overview. *International ophthalmology* 2017; 1-9.
- 2 Pinazo-Durán MD, Pons-Vázquez S, Gallego-Pinazo R, Estrada CG, Zanón-Moreno V, Bou VV, *et al* — Thyroid hormone deficiency disrupts rat eye neurodevelopment. *Brain research* 2011; **1392**: 16-26.
- 3 Bilgihan K, Bilgihan A, Diker S, Ataoglu O, Dolapci M, Akata F, *et al* — Effects of hyper- and hypothyroidism on oxidative stress of the eye in experimental acute anterior uveitis. *Acta Ophthalmologica* 1996; **74**: 41-3.
- 4 Miller PE, Panciera DL. Effects of experimentally induced hypothyroidism on the eye and ocular adnexa of dogs. *American journal of veterinary research* 1994; **55**: 692-7.
- 5 Mahto RS — Ocular features of hypothyroidism. *The British Journal of Ophthalmology* 1972; **56**: 546.
- 6 Kan E, Kiliçkan E, Ecemis G, Beyazyildiz E, Çolak R — Presence of Dry Eye in Patients with Hashimoto's Thyroiditis. *Journal of ophthalmology*. 2014; <http://dx.doi.org/10.1155/2014/754923>
- 7 Gatziofuz Z, Panos GD, Brugnolli E, Hafezi F — Corneal topographical and biomechanical variations associated with hypothyroidism. *Journal of Refractive Surgery* 2014; **30**: 78-9.
- 8 Tabibian D, de Tejada BM, Gatziofuz Z, Kling S, Meiss VS, Boldi MO, *et al* — Pregnancy-induced changes in corneal biomechanics and topography are thyroid hormone related. *American Journal of Ophthalmology* 2017; **184**: 129-36.
- 9 Thanos S, Oellers P, Zu Hörste MM, Prokosch V, Schlatt S, Seitz B, Gatziofuz Z — Role of thyroxine in the development

- of keratoconus. *Cornea* 2016; **35**: 1338-46.
- 10 Gatzoufas Z, Thanos S — Acute keratoconus induced by hypothyroxinemia during pregnancy. *Journal of Endocrinological investigation* 2008; **31**: 262-6.
  - 11 Wang S, Liu Y, Zheng G — Hypothyroidism as a risk factor for open angle glaucoma: A systematic review and meta-analysis. *PloS one* 2017; **12**: e0186634.
  - 12 Lee AJ, Rochtchina E, Wang JJ, Healey PR, Mitchell P — Open-angle glaucoma and systemic thyroid disease in an older population: The Blue Mountains Eye Study. *Eye* 2004; **18**: 600-8.
  - 13 Lin HC, Kang JH, Jiang YD, Ho JD — Hypothyroidism and the risk of developing open-angle glaucoma: a five-year population-based follow-up study. *Ophthalmology* 2010; **117**: 1960-6.
  - 14 Gleeson H, Kelly W, Toft A, Dickinson J, Kendall-Taylor PA, Fleck B, *et al* — Severe thyroid eye disease associated with primary hypothyroidism and thyroid-associated dermopathy. *Thyroid* 1999; **9**: 1115-8.
  - 15 Fox RA, Schwartz TB — Infiltrative ophthalmopathy and primary hypothyroidism. *Annals of Internal Medicine* 1967; **67**: 377-80.
  - 16 Aharon A, Zandman-Goddard G, Shoenfeld Y — Autoimmune multiorgan involvement in elderly men is it SLE? *Clinical rheumatology* 1994; **13**: 631-4.
  - 17 Chong KK, Lai TH, Chan R, Li CL, Young A — Thyroid eye disease: a 2017 update from the first thyroid eye clinic in Hong Kong. *Hong Kong Journal of Ophthalmology* 2017; **21**: 11-8.
  - 18 Walsh JP, Dayan CM, Potts MJ — Radioiodine and thyroid eye disease: Use with caution. *British Medical Journal* 1999; **319**: 68.
  - 19 Bromfield S, Keenan J, Jolly P, McGwin Jr G — A suggested association between hypothyroidism and age-related macular degeneration. *Current Eye Research* 2012; **37**: 549-52.
  - 20 Campos SP, Olitsky S — Idiopathic intracranial hypertension after L-thyroxine therapy for acquired primary hypothyroidism. *Clinical Pediatrics* 1995; **34**: 334-7.
  - 21 Stirn Kranjc B — Ocular Abnormalities and Systemic Disease in Down Syndrome: Retrospective clinical study, University Eye Hospital, Ljubljana, Slovenia. *Strabismus* 2012; **20**: 74-7.
  - 22 Comi AM, Bellamkonda S, Ferenc LM, Cohen BA, Germain-Lee EL — Central hypothyroidism and Sturge-Weber syndrome. *Pediatric Neurology* 2008; **39**: 58-62.
  - 23 Jaggarao N, Voth D, Jacobsen J — The Vogt-Koyanagi-Harada syndrome: association with hypothyroidism and diabetes mellitus. *Postgraduate Medical Journal* 1989; **65**: 587-8.
  - 24 Kosaki R, Kamiishi A, Sugiyama R, Kawai M, Hasegawa T, Kosaki K — Congenital hypothyroidism in Peters plus syndrome. *Ophthalmic Genetics* 2006; **27**: 67-9.
  - 25 Lei S, Iyengar S, Shan L, Cherwek DH, Murthy S, Wong AM — GAPO syndrome: a case associated with bilateral interstitial keratitis and hypothyroidism. *Clinical Dysmorphology* 2010; **19**: 79-81.
  - 26 Gordon LK — Orbital inflammatory disease: a diagnostic and therapeutic challenge. *Eye* 2006; **20**: 1196-206.
  - 27 Pivnick EK, Velagaleti GV, Wilroy RS, Smith ME, Rose SR, Tipton RE, *et al* — Jacobsen syndrome: report of a patient with severe eye anomalies, growth hormone deficiency, and hypothyroidism associated with deletion 11 (q23q25) and review of 52 cases. *Journal of Medical Genetics* 1996; **33**: 772-8.
  - 28 Frieden IJ, Reese V, Cohen D — PHACE syndrome: the association of posterior fossa brain malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and eye abnormalities. *Archives of Dermatology* 1996; **132**: 307-11.
  - 29 Senée V, Chelala C, Duchatelet S, Feng D, Blanc H, Cossec JC, *et al* — Mutations in GLIS3 are responsible for a rare syndrome with neonatal diabetes mellitus and congenital hypothyroidism. *Nature Genetics* 2006; **38**: 682-7.