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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Original Research Article

Study on relationship between intraocular pressure and hyperthyroidism

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ARTICLE INFO

Article history:
Received 19-02-2022
Accepted 22-03-2022
Available online 29-09-2023

Keywords:
Glaucoma
Hypothyroidism
Population based
Thyroxine
Thyroid disease

ABSTRACT

Background: Thyroid-associated ophthalmopathy (TAO) represents a persistent autoimmune inflammatory condition impacting various ocular components, including orbital fat (OF), extraocular muscles (EOMs), the eyeball, and associated eye structures. This disorder is closely associated with autoimmune thyroid pathology. A body of research has indicated an elevated susceptibility to heightened intraocular pressure (IOP) and glaucoma among individuals with thyroid-related ailments. Nonetheless, certain studies have expressed reservations about affirming these conclusions. Furthermore, there exists a diversity of viewpoints regarding the optimal approaches for managing elevated IOP in TAO patients afflicted with ocular hypertension

Materials and Methods: A prospective research investigation was undertaken within the Department of Ophthalmology at a Tertiary Care Teaching Hospital, spanning a duration of 12 months. The techniques employed for the diagnosis of open-angle glaucoma (OAG) have been comprehensively outlined. Goldmann applanation tonometry was utilized to determine intraocular pressure (IOP). Employing a Zeiss FF3 fundus camera, a series of dilated stereoscopic 300-color retinal and optic disc images were captured. The evaluation of optic disc photographs was conducted by one of two evaluators, both of whom remained masked to the study's particulars, employing a customized protocol. In order to ascertain optic disc dimensions, adjustments for camera magnification were performed, accounting for the spherical equivalent refraction of each individual eye.

Result: A total of 90 patients were examined. Of the 90 cases, male preponderance was noted. Among 90 patients, 20 (22.2%) were hyperthyroid, 61 (67.8%) were hypothyroid, and 9 (10%) patients were euthyroid. In our study shows the frequency of different symptoms among the study group. Most of the patients came with complaint itching of (27.8%). The second most common symptom was foreign body sensation (21.1%). In this study shows the different types of signs among these two groups. In hyperthyroid lid, retraction was more common (12%). In hypothyroid lid, edema was more common (18.5%). Frequency of dry eye syndrome in patients with TD was present; 29 (26.4%) patients had dry eye disease. Among 90 patients, proptosis was present in 4 patients had proptosis. Most of the patients were myopic.

Conclusion: Our results imply the potential link between intraocular pressure (IOP) and thyroid-related disorders, particularly in individuals undergoing thyroxine treatment. Conducting further comprehensive investigations to explore and substantiate this prospective association is advisable.

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1. Introduction

Thyroid-associated ophthalmopathy (TAO) is a chronic autoimmune inflammatory ailment that impacts the

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https://doi.org/10.18231/j.ijceo.2023.083
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orbital fat (OF), extraocular muscles (EOMs), eyeball, and associated eye structures, interconnected with thyroid autoimmune pathology.[1] Clinical manifestations encompass widened palpebral fissure, eyelid retraction, conjunctival hyperemia, exophthalmos, corneal exposure, restrictive myopathy, optic neuropathy, and additional symptoms.[2] Typically, the ocular manifestations tend to be mild, with the severe form of the disorder affecting a minority, about 3% to 5% of individuals.[3]

Numerous investigations have highlighted a heightened susceptibility to elevated intraocular pressure (IOP) and glaucoma among individuals with thyroid disorders.[4] However, certain studies have voiced scepticism concerning these conclusions. Cockerham's study indicated that while a quarter of TAO patients exhibited ocular hypertension, occurrences of glaucoma-related damage were infrequent and even lower than the relative risk observed for glaucoma visual field defects in healthy individuals.[5] Discrepancies also exist regarding optimal approaches for mitigating elevated IOP in TAO patients with ocular hypertension. Despite various theoretical frameworks, the interplay between ocular hypertension, open-angle glaucoma, and TAO remains enigmatic. Elevated IOP in TAO may be attributed to inflammation-induced expansion of EOMs, leading to constriction and compression of the eyeball.[6] Furthermore, reduced orbital venous drainage could elevate episcleral venous pressure, or increased mucopolysaccharide deposition within the trabecular meshwork might hinder aqueous humour outflow.[7]

Research has identified a range of systemic and ocular risk factors associated with the co-occurrence of TAO and open-angle glaucoma, including advanced age, female gender, familial glaucoma history, myopia, diabetes, hypertension, presence of pseudoexfoliation, and thyroxine treatment. Numerous factors also influence IOP levels in TAO patients.[8] The present study encompassed individuals with elevated IOP in a single eye and compared variables such as EOMs and the clinical activity score (CAS) between the two eyes. This examination delved into the factors contributing to heightened IOP in TAO patients, aiming to inform future treatment decisions. Notably, the study effectively mitigated confounding influences, encompassing variables like age, gender, blood pressure, measurement timing, medication history, thyroid hormone status, and presence of other systemic disorders among individuals exhibiting elevated IOP.

2. Materials and Methods

This prospective study was conducted within the Department of Ophthalmology at a Tertiary Care Teaching Hospital, spanning a duration of one year.

The diagnostic methodologies employed to identify Open-Angle Glaucoma (OAG) have been explicated. Intraocular pressure (IOP) measurements were obtained through Goldmann applanation tonometry. Dilated stereoscopic 300-color retinal and optic disc photographs were captured using a Zeiss FF3 fundus camera. The grading of optic disc photographs was conducted by one of two masked graders, employing a modified protocol. For precise measurement of optic disc dimensions, camera magnification was adjusted through the utilization of the spherical equivalent refraction corresponding to each eye.

Screening automated perimetry was conducted on subjects. Among these participants, individuals were categorized as glaucoma suspects if they exhibited field defects, displayed a glaucomatous appearance of the optic disc, or possessed a past history of glaucoma or ocular hypertension. Subsequent to this initial screening, these subjects underwent Humphrey 30-2 full-threshold visual field tests and gonioscopy assessment.

The minimum diagnostic criteria for Open-Angle Glaucoma (OAG) entailed an abnormal Humphrey 30-2 Glaucoma Hemifield Test, coupled with one or more of the ensuing field defects not attributable to ocular or neurological causes: (1) arcuate or paracentral scotoma, (2) nasal step, or (3) advanced glaucomatous field loss. The definitive diagnosis of OAG was rendered upon concordance between characteristic glaucomatous visual field loss on the Humphrey 30-2 tests and optic disc rim loss evident in stereo photographs, following exclusion of angle closure, rubeosis, or secondary glaucoma, barring pseudoexfoliation. Low-pressure glaucoma (LPG) encompassed cases devoid of ocular hypotensive medication usage or prior glaucoma surgery, with both eyes' Intraocular Pressure (IOP) maintained below 21 mmHg. Contrastingly, other glaucoma instances were designated as high-pressure glaucoma (HPG). Ocular hypertension (OH) was diagnosed among subjects lacking distinctive glaucomatous disc or field alterations, or secondary glaucoma, yet exhibiting IOP surpassing 22 mmHg.

A thorough medical and familial history was elicited, encompassing a record of glaucoma in first-degree relatives. Systemic hypertension was defined as a history of elevated blood pressure, ongoing antihypertensive treatment, or systolic blood pressure exceeding 160 mmHg and/or diastolic blood pressure surpassing 95 mmHg.

Thyroid disease history was meticulously ascertained, including its origin, age of diagnosis, and thyroid activity at diagnosis. Particulars regarding thyroid treatment and its duration were meticulously documented. The usage of thyroid medication was corroborated via a dedicated query encompassing current and past medication regimens. Thyroid status was stratified into three distinct categories based on reported thyroid activity at diagnosis. Participants diagnosed with hypoactive or hyperactive thyroid conditions at diagnosis were classified as 'hypothyroid' and 'hyperthyroid', correspondingly. Those subjects presenting with thyroid nodules, adenomas, cysts, goiters, carcinomas,

or cases where the thyroid activity at diagnosis couldn't be established were categorized as 'unspecified'. Further categorization of thyroid subjects was executed based on the scope of treatment received, encompassing thyroxine (current or past), past I131 treatment, past thyroid surgery, and usage of antithyroid medication (propylthiouracil or carbimazole). In both age-and sex-adjusted as well as multivariate analyses, the reference group consisted of subjects without thyroid disease (n= 3330), while the subgroup under thyroid scrutiny constituted the focus of analysis.

2.1. Data analysis

All statistical computations, encompassing the utilization of the chi-squared statistic, the Mantel–Haenszel chi-squared test, and logistic regression analyses, were executed employing the Statistical Analysis System (SAS). The multiple logistic regression models incorporated a selection of potential confounding variables, comprising age (continuous), gender, family history of glaucoma, diabetes, hypertension, myopia, and pseudoexfoliation. The outcomes were conveyed through odds ratios (OR) and their corresponding 95% confidence intervals (CI). Statistical significance was established at a threshold of $p < 0.05$.

3. Results

A total of 90 patients were examined. Of the 90 cases, male preponderance was noted as shown in Table 1.

Table 1: Sex distribution of patients

Sex	No. of patients	Percentage
Male	38	42.2
Female	52	57.8
Total	90	100

Table 2: Age distribution of patients

Age group	No. of patients	Percentage
<20	9	10
21-40	28	31.1
41-60	39	43.3
>61	14	15.6
Total	90	100

According to Table 2, 41-60 years age group had the highest incidence of thyroid orbitopathy, the patients were arbitrarily divided into four groups and least one less than 20 years of age group.

Within Table 3, a total of 90 patients was analysed, revealing that 20 individuals (22.2%) exhibited hyperthyroidism, while the majority, comprising 61 patients (67.8%), displayed hypothyroidism. Additionally, nine patients (10%) were classified as euthyroid.

Table 3: Ocular manifestations

Thyroid status	No. of patients	Percentage
Hyperthyroid	20	22.2
Hypothyroid	61	67.8
Euthyroid	9	10
Total	90	100

Table 4: Severity of thyroid-associated ophthalmopathy

Severity of TAO	No. of patients	Percentage
Mild	58	64.4
Moderate	23	25.6
Severe	9	10
Total	90	100

Table 5: Symptoms of thyroid eye disease patients

Sign	No. of patients	Percentage
Itching	25	27.8
Foreign body sensation	19	21.1
Dry eye	11	12.2
Lid swelling	9	10
Redness	8	8.9
Difficulty in reading	7	7.8
Protrusion of eye	5	5.6
Diminution of vision	3	3.3
Watering	3	3.3

Table 5 delineates the prevalence of distinct symptoms within the study cohort. Notably, a significant proportion of patients reported experiencing itching, constituting 27.8% of the total. Subsequently, the second most prevalent symptom manifested as a foreign body sensation, accounting for 21.1% of the cases.

Table 6: Ocular signs in hyperthyroidism patient

Sign	Hyperthyroid, N=25 (%)	Hypothyroid, N=65 (%)
Lid edema (Enroth's sign)	1 (4)	12 (18.5)
Lid retraction (Dalrymple sign)	3 (12)	-
Lid lag (Graefe's sign)	2 (8)	-
Conjunctival congestion	1 (4)	3 (4.6)
Corneal ulcer	1 (4)	4 (6.1)
Proptosis	4 (16)	-
Scleral show	2 (8)	-
Increased palpebral aperture	3 (12)	-
Restrictive myopathy	5 (20)	-
Refractive error	1 (4)	46 (70.8)
Increase IOP with optic disk and visual field change	2 (8)	-

Table 6 illustrates the varying manifestations within these two distinct groups. Within the hyperthyroid lid subgroup,

retraction emerged as a predominant feature, being observed in 12% of cases. Conversely, in the hypothyroid lid subgroup,edema assumed a more prevalent role, accounting for 18.5% of occurrences. Dry eye syndrome exhibited a noteworthy prevalence among patients with thyroid dysfunction, with 29 individuals (26.4%) presenting with this condition. Out of the total cohort of 90 patients, proptosis was discerned in merely 4 cases. Furthermore, a substantial portion of the patient population demonstrated myopia as a prevailing ocular characteristic.

4. Discussion

Based on a nationally-representative, population-based cohort, this study has demonstrated a significant association between self-reported thyroid issues and Intraocular Pressure (IOP), even after adjusting for demographic factors and smoking habits. Several prior investigations have also highlighted noteworthy connections between open-angle glaucoma and thyroid disorders[9] However, a significant proportion of these antecedent investigations were conducted with limited, specialised clinic-based samples, thereby rendering them susceptible to selection bias emanating from referral mechanisms. By contrast, a substantial population-based study in Australia unveiled a noteworthy correlation between open-angle glaucoma, individuals under thyroxine treatment, and those with a history of thyroid surgery. Notably, this Australian study predominantly encompassed subjects of Caucasian descent. Simultaneously, it is imperative to acknowledge that several empirical inquiries have not substantiated a statistically significant association.[10]

Notwithstanding these limitations, the plausibility of a connection persists due to several hypothesized mechanisms that link different thyroid conditions to IOP. For instance, in the case of hypothyroidism, a prevalent thyroid disorder, the deposition of mucopolysaccharides in the trabecular meshwork is anticipated, resulting in heightened IOP and increased resistance to aqueous outflow.[11] This hypothesis gains support from postmortem investigations involving both animal and human eyes, which were subjected to hyaluronidase perfusion in the anterior chamber.[12] Furthermore, individuals with hypothyroidism who underwent thyroid replacement therapy demonstrated enhancements in IOP and increased outflow facility.[13]

Therefore, the outcomes of this study hold significance as they provide backing, from a nationally representative multiracial/ethnic sample, for the proposition that thyroid disorders could potentially serve as an autonomous risk factor for IOP. Additionally, it is worth noting that in unreported results, we observed minimal racial variations concerning the impact of thyroid disorders on IOP.

The implications of these findings should be considered within the framework of several inherent limitations. The dependency on self-reported data introduces the possibility of misclassification. Investigations assessing the accuracy of self-report compared to medically confirmed diagnoses have consistently revealed a noteworthy trend of IOP underreporting and hyperthyroidism/hypothyroidism overreporting.[14] Previous research suggests that underreporting of IOP may be due to lack of awareness, and overreporting of hyper- and hypothyroidism could stem from misclassification. These reporting errors introduce a non-differential misclassification bias, likely causing an underestimation of the associations between these disease categories, despite the significant observed associations in our study.

Furthermore, comprehensive data pertaining to the precise subtype of Intraocular Pressure (IOP) irregularities and/or specific types of thyroid disorders manifested, alongside their respective severity and durations, remains available. Consequently, although Open-Angle Glaucoma (OAG) and hypothyroidism emerge as prevalent pathological conditions within their respective domains, discerning the exact nature of thyroid or glaucomatous afflictions linked to this study proves to be a challenging endeavor. Previous research endeavors have revealed compelling correlations between Open-Angle Glaucoma and hypothyroidism, Graves' disease, individuals currently under thyroxine medication, and those with a history of thyroid surgery.[15] Moreover, the chronological sequence regarding the onset of thyroid abnormalities and Intraocular Pressure (IOP) variations still needs to be determined within the scope of this study. Addressing this matter, the absence of data regarding ongoing or prior therapeutic interventions for thyroid dysfunctions (such as medication regimens or surgical procedures) is noteworthy. This omission holds significance in the investigative context, as certain thyroid disorders, including hypothyroidism, are relatively prevalent and amenable to effective treatment strategies. Consequently, exploring potential intervention measures assumes relevance, given the potential for favourable outcomes.

5. Conclusion

Our study outcomes propose the potential existence of a correlation between intraocular pressure (IOP) and thyroid-related disorders, with a notable emphasis on individuals undergoing thyroxine treatment. This discovery prompts a more comprehensive investigation into this potential link. Subsequent exploration will help establish the extent and nature of the association between IOP and thyroid disease in subjects treated with thyroxine, shedding light on possible clinical implications and therapeutic interventions.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Gitanjali M, Chowdary S, Sultana SS, Fatima SW. Study on relationship between intraocular pressure and hyperthyroidism. *Indian J Clin Exp Ophthalmol* 2023;9(3):436-440.