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The Association between Thyroid Problems and Glaucoma

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Abstract

Aims—To evaluate the association between thyroid problems and glaucoma.

Methods—A population-based cross-sectional sample with 12,376 participants from the 2002 National Health Interview Survey (NHIS). Odds ratios (OR) and 95% confidence intervals (CI) were used to quantify the association between a self-reported diagnosis of glaucoma and a self-reported history of thyroid problems, controlling for demographic characteristics and smoking status.

Results—The overall prevalence of glaucoma was 4.6%; 11.9% reported a history of thyroid problems. The prevalence of glaucoma among those who did and did not report thyroid problems was 6.5% and 4.4%, respectively ($p=0.0003$). Following adjustment for differences in age, gender, race, and smoking status, the association between glaucoma and thyroid problems remained (OR 1.38, 95% CI 1.08-1.76).

Conclusions—The results of this study lend support to the hypothesis that thyroid disorders may increase the risk of glaucoma. Research should continue evaluating potential mechanisms underlying this relationship and whether the treatment of thyroid problems reduces subsequent glaucoma risk.

INTRODUCTION

Primary open angle (OAG) glaucoma is a leading cause of vision impairment and blindness in the United States and worldwide.[1] The incidence of glaucoma increases with age, and it is higher among African-Americans than most other racial and ethnic groups.[1-3] As a broad category, thyroid condition may potentially have an effect on the development of glaucoma. Several case reports and case series have found an association with hypothyroidism,[4-8] and a recent population-based study found that glaucoma was more common among thyroxine users and those with a history of thyroid surgery.[9] However, that study was comprised of Australian's largely of European ancestry, thus limiting the generalizability of the results. Other studies, however, have failed to find a significant association between hypothyroidism and glaucoma.[10-13] Thus, there is a lack of consistent epidemiologic evidence on associations between hypothyroidism and glaucoma. Additionally, though considerably less common, significant relationships have been demonstrated between thyroid-associated orbitopathy

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(Graves orbitopathy/ophthalmology) and open-angle glaucoma and ocular hypertension (OHT).[14-16]

Glaucoma is characterized by progressive optic nerve damage, resulting in the death of retinal ganglion cells, which ultimately impedes the transmission of visual impulses from the eye to the brain.[2] Although elevated intraocular pressure (IOP) is a primary risk factor, glaucomatous injury may occur at normal IOP.[3] There are a number of purported mechanisms by which thyroid disorders and their treatment are believed to affect the development of glaucomatous damage. In Graves disease, IOP may be raised as a result of contraction of the extraocular muscles against intraorbital adhesions or orbital congestion due to increased tissue volumens.[16-17] In the case of hypothyroidism, excessive mucopolysaccharide accumulation within the trabecular meshwork acts like a surfactant, sticking together adjacent endothelial membranes.[9] The purpose of this study is to determine, in a large American population-based cohort of participants, if thyroid problems are associated with glaucoma.

MATERIALS AND METHODS

Data Source

The data used for this study are drawn from the 2002 National Health Interview Survey (NHIS), which serves as the principal source of health information of the civilian, non-institutionalized, household population of the United States, and it represents a key data collection program of the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC).[18] Since its inception in 1957, the NHIS has used a repeated cross-section, multistage, stratified, cluster design to annually collect health information on tens of thousands of persons in the United States. Specifically, for the NHIS Sample Adult questionnaire, one adult member per family is randomly chosen to provide information on themselves. When weighted, the data are nationally representative of the non-institutionalized civilian U.S. population.

Variable Definitions

As part of the Sample Adult component, all study participants were asked whether they had ever been told by a doctor or other healthcare professional that they had a thyroid problem. Likewise, study participants were asked whether a physician or other healthcare professional had ever told them they have glaucoma. Data on demographic characteristics (i.e., age, gender, race) and smoking status, which may confound the association between thyroid problems and glaucoma, were also collected and included in analyses.

Statistical Analysis

To account for the stratified clustered design of the survey, the PROC SURVEY procedures in SAS (SAS Institute, Cary, NC, USA) were employed for data description and analyses. Respondents with and without thyroid problems were compared with respect to demographic characteristics, smoking status, and glaucoma using Rao-Scott Modified chi-squared tests and *t*-tests for categorical and continuous variables. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between thyroid problems and glaucoma with and without adjustment for demographic characteristics and smoking status. All statistical tests were performed at the 5% level of significance.

RESULTS

Approximately 12% of the participants reported ever having been told by a doctor or health professional that they had thyroid problems. On average, those with thyroid problems were older and more likely to be female and white compared to those who did not report having

thyroid problems (Table 1). There were proportionately more former or never smokers among those who reported thyroid problems compared to those who did not. The prevalence of self-reported glaucoma was significantly higher among those who reported a history of thyroid problems compared to those who did not (6.5% vs. 4.4%, respectively; $p=.0003$).

Unadjusted and adjusted logistic regression results are presented in Table 2. The unadjusted results demonstrate that glaucoma is associated with older age, females, and African Americans. After adjusting for all covariates, compared to current smokers, those who never smoked were nearly equally as likely to have glaucoma, and former smokers were somewhat more likely to have glaucoma; however, none of these differences are statistically significant. Consistent with the results in Table 1, thyroid problems are significantly associated with glaucoma (OR 1.53; 95% CI 1.22-1.93). Following adjustment for age, gender, race and smoking status, the association between thyroid problems and glaucoma is attenuated, but remains statistically significant (OR 1.38; 95% CI 1.08-1.76).

DISCUSSION

Using a nationally-representative, population-based sample, this study found a significant relationship between self-reported thyroid problems and glaucoma, even after controlling for demographic characteristics and smoking status. Several past studies have found significant associations between open-angle glaucoma and thyroid disorders.[4-7,14,16] However, many of these studies were comprised of small, specialty-clinic based samples, which may be affected by selection bias from referral mechanisms. A large Australian, population-based study also found a significant association between open-angle glaucoma with thyroxine users and those with a history of thyroid surgery, but it was predominantly comprised of Caucasians. At the same time, several investigations have not found a significant relationship.[10-13] Despite these limitations, a relationship remains plausible because there are several hypothesized mechanisms linking various types of thyroid conditions and glaucoma. A common thyroid condition, hypothyroidism, may lead to the deposition of mucopolysaccharides in the trabecular meshwork, which increases IOP as well as aqueous outflow resistance.[19-20] Postmortem studies using animal and human eyes perfused with hyaluronidase in the anterior chamber support this hypothesis.[21-22] Moreover, patients with hypothyroidism who received thyroid replacement medication have exhibited improved IOP as well as outflow facility.[5] Thus, the findings in the present study are important because, based on a nationally-representative multiracial/ethnic sample, it lends support to the notion that thyroid disorders may be an independent risk factor for glaucoma. In results not shown, we did not find substantial racial differences across the effects of thyroid disorders on glaucoma.

These results must be interpreted in light of several limitations. The reliance on self-report may result in misclassification. Indeed, studies examining the validity of self-report compared to confirmed diagnosis indicate that there is considerable underreporting of glaucoma[23] and overreporting of hyperthyroidism and hypothyroidism.[24] Such research suggests that glaucoma is underreported because people are unaware they have it, and hyper- and hypothyroidism are overreported among people who in fact have another kind of thyroid disorder, and also among those completely healthy. However, these reporting errors are likely to impart a non-differential misclassification bias and thus shift estimates of risk towards that null. Given the significant associations seen in this study, this implies that the estimates of association between these categories of disease may be underestimated.

Further, data on the specific type of glaucoma and/or thyroid disorder present, as well as their severity and duration, is not available. Thus, while OAG and hypothyroidism are common disease states within each category, it is not possible to determine which specific thyroid or glaucomatous condition or conditions are associated. Research has found associations between

OAG with hypothyroidism,[4-6] Graves disease,[16] those currently taking thyroxine,[9] and those with a history of thyroid surgery.[9] Also, the temporal relationship between thyroid problems and glaucoma cannot be established in the present study. Related to this issue, information on current or past treatment for thyroid problems (e.g., medication, surgery) was not included, so we could not determine whether such treatments prevent or slow down the development of glaucoma. This is important to investigate because some thyroid disorders, such as hypothyroidism, are fairly prevalent but easily treatable so intervention efforts may be worthwhile.

Despite these limitations, this large national-representative sample provides important evidence of a possible association between these two disease categories, particularly considering that the preexisting literature mainly consists of a few small case-control studies that have yielded conflicting results. The association between thyroid disorders and the development of glaucoma is important to establish, given the high prevalence of both conditions in the general population. Thus, prospective research is warranted on the development of glaucoma and thyroid disorders to more definitively ascertain whether thyroid problems instigate and/or exacerbate glaucomatous damage.

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Table 1

Demographic, Smoking Status, and Glaucoma Differences Between Those Who Had Thyroid Problems and Those Who Did Not Have Thyroid Problems (n=12,376)

	Thyroid Problems		p-value
	No	Yes	
Age, mean	63.7	66.1	<0.0001
Female, %	50.5	81.0	<0.0001
Race, %			<0.0001
White	79.4	87.4	
Hispanic	9.5	5.8	
Black	7.6	4.6	
Other	3.4	2.2	
Smoker, %			0.0003
Current	16.2	12.4	
Former	35.1	37.2	
Never	47.5	50.0	
Unknown	1.2	0.4	
Glaucoma, %	4.4	6.5	0.0003

Table 2
Unadjusted and Adjusted Logistic Regression Models Estimating Thyroid Problems on Glaucoma

	Unadjusted		Adjusted ^b	
	OR	95% CI	OR	95% CI
Age	1.07 ***	1.06-1.08	1.07 ***	1.06-1.08
Female	1.21 *	1.01-1.46	1.07	0.88-1.31
Race				
White	1.00		1.00	
Hispanic	0.94	0.68-1.30	1.15	0.83-1.68
Black	2.02 ***	1.57-2.60	2.43 ***	1.87-3.16
Other	0.80	0.43-1.51	1.01	0.52-1.94
Smoking Status				
Current	1.00		1.00	
Former	1.77	1.30-2.42	1.29	0.94-1.77
Never	1.54	1.13-2.09	1.06	0.77-1.46
Unknown	2.56	1.91-5.49	1.67	0.78-3.62
Thyroid problems	1.53 ***	1.22-1.93	1.38 **	1.08-1.76

^b This column represents the simultaneous adjusted regression of glaucoma on all variables.

*
p<.05

**
p<.01

p<.001