

INVESTIGATING THE RELATIONSHIP BETWEEN HYPOTHYROIDISM AND PRIMARY OPEN ANGLE GLAUCOMA: A CASE-CONTROL STUDY

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ABSTRACT:

Background: Hypothyroidism and primary open-angle glaucoma (POAG) are common disorders affecting various systems of the body, including the endocrine and visual systems. While previous studies have suggested a potential association between hypothyroidism and POAG, the precise nature of this relationship remains unclear. This case-control study aims to investigate the association between hypothyroidism and the risk of developing POAG.

Methods: A total of 50 participants were enrolled in this study, comprising 25 individuals with hypothyroidism and 25 age- and sex-matched controls without hypothyroidism. All participants underwent comprehensive ophthalmic examination, including intraocular pressure measurement, optic nerve head assessment, and visual field testing. Clinical data, including thyroid function tests, were collected from medical records. The association between hypothyroidism and POAG was analyzed using appropriate statistical methods, adjusting for potential confounders.

Results: Among the 25 participants with hypothyroidism, 8 (32%) were diagnosed with POAG, whereas only 2 (8%) of the control group had POAG. The difference in the prevalence of POAG between the two groups was statistically significant ($p < 0.05$). After adjusting for age, sex, and other potential confounders, hypothyroidism was found to be independently associated with a significantly higher risk of developing POAG, with an odds ratio of 4.50 (95% confidence interval: 1.32–15.34, $p = 0.017$).

Conclusion: This case-control study provides evidence of a significant association between hypothyroidism and the risk of developing POAG. These findings suggest that individuals with hypothyroidism may have an increased susceptibility to POAG, highlighting the importance of regular ophthalmic screening in this population. Further research is warranted to elucidate the underlying mechanisms linking hypothyroidism and POAG and to explore potential therapeutic interventions targeting this association.

Keywords: *Hypothyroidism, primary open-angle glaucoma, case-control study, association, risk factor, ophthalmic screening.*

Introduction:

Hypothyroidism, characterized by insufficient thyroid hormone production, and primary open-angle glaucoma (POAG), a leading cause of irreversible blindness worldwide, are both prevalent disorders with multifactorial etiologies. Previous research has suggested a potential association between hypothyroidism and POAG, although the underlying mechanisms remain

unclear^[1]. The aim of this study is to investigate the association between hypothyroidism and the risk of developing POAG through a case-control study design.

Hypothyroidism is a common endocrine disorder affecting approximately 4.6% of the U.S. population, with higher prevalence among women and the elderly^[2]. The condition results from insufficient thyroid hormone production by the thyroid gland, leading to a range of systemic manifestations including fatigue, weight gain, cold intolerance, and cognitive impairment. Moreover, hypothyroidism has been implicated in various ocular manifestations, including dry eye syndrome, ophthalmoplegia, and optic neuropathy^[3].

POAG is the most prevalent form of glaucoma globally and a leading cause of irreversible blindness, particularly in the elderly population^[4]. It is characterized by progressive damage to the optic nerve and visual field loss, often in the absence of elevated intraocular pressure (IOP). While the exact pathophysiology of POAG remains incompletely understood, several risk factors have been identified, including elevated IOP, age, family history, and myopia^[5].

Despite the substantial burden of both hypothyroidism and POAG on public health, limited research has been conducted to explore their potential association. A few epidemiological studies have suggested a possible link between thyroid dysfunction and glaucoma, albeit with conflicting results^[1,6]. The underlying mechanisms by which thyroid dysfunction might influence the development or progression of POAG remain speculative but could involve vascular compromise, oxidative stress, or neurodegenerative processes^[7].

Understanding the potential relationship between hypothyroidism and POAG holds significant clinical and public health implications. Firstly, if a significant association is identified, it could have implications for screening and management strategies in patients with hypothyroidism. Early detection of POAG in this population may enable timely intervention to prevent irreversible vision loss. Secondly, elucidating the underlying mechanisms linking thyroid dysfunction and glaucoma could provide insights into the pathogenesis of POAG, potentially leading to novel therapeutic targets. Finally, given the high prevalence of both conditions, clarifying their relationship could inform healthcare policy and resource allocation to optimize patient care and reduce the socioeconomic burden associated with vision impairment^[8].

In this context, the present study aims to fill the existing gap in knowledge by conducting a case-control investigation into the association between hypothyroidism and POAG. By systematically evaluating a range of potential risk factors and clinical implications, this study seeks to contribute to a better understanding of the interplay between thyroid function and ocular health.

Aims and objectives:

The primary objective of this study is to determine whether there is a significant association between hypothyroidism and the prevalence of POAG. Secondary objectives include evaluating potential risk factors for POAG within the hypothyroid population and assessing the clinical implications of any observed association.

Materials and methods:

Study Design: This case-control study was conducted to investigate the association between hypothyroidism and primary open-angle glaucoma (POAG).

Study Participants: A total of 50 participants were enrolled, comprising 25 individuals diagnosed with hypothyroidism and 25 age- and sex-matched controls without hypothyroidism.

Participants were recruited from tertiary care hospital in Tamil Nadu between August 2022-Jan 2023

Sampling Procedure: Participants were recruited from tertiary care hospital in Tamil Nadu, ensuring representation from both outpatient clinics and inpatient departments. The selection of participants with hypothyroidism and controls without hypothyroidism was conducted using a systematic sampling method. Individuals diagnosed with hypothyroidism were identified from medical records, while age- and sex-matched controls without hypothyroidism were randomly selected from the same population pool.

Sample Size: A sample size of 50 participants was determined based on power analysis, considering an estimated effect size derived from previous studies^[6] investigating the association between hypothyroidism and POAG. This sample size was deemed adequate to detect a clinically significant difference in the prevalence of POAG between individuals with hypothyroidism and controls, with a power of 80% and a significance level of 0.05. The sample size calculation was performed using statistical software, taking into account the anticipated dropout rate and potential confounding variables.

Data Collection: Detailed demographic information, medical history, and clinical data were collected from all participants. Thyroid function tests, including serum levels of thyroid-stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3), were obtained from medical records for participants with hypothyroidism. Ophthalmic examinations were performed on all participants, including intraocular pressure (IOP) measurement using Goldmann applanation tonometry, optic nerve head assessment using slit-lamp biomicroscopy, and visual field testing using automated perimetry.

Case Definition: Hypothyroidism was defined as elevated TSH levels with decreased T4 and/or T3 levels, consistent with clinical guidelines. POAG was diagnosed based on characteristic optic nerve head changes, visual field defects consistent with glaucoma, and open anterior chamber angles on gonioscopy.

Statistical Analysis: Data were analyzed using appropriate statistical methods, including chi-square test or Fisher's exact test for categorical variables and t-test or Mann-Whitney U test for continuous variables, as applicable. Logistic regression analysis was performed to assess the association between hypothyroidism and the risk of developing POAG, adjusting for potential confounders such as age, sex, and other relevant variables.

Ethical Considerations: This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board (IRB)/Ethics Committee of Sree Mookambika Institute of Medical Sciences. Informed consent was obtained from all participants prior to enrollment in the study.

Results:

Table 1: Baseline Characteristics of Study Participants

Baseline Characteristics	Cases (n=25)	Control (n=25)
Age (years),	45.6 ± 8.2	45.4 ± 7.9
Sex (Male/Female), n	7/18	7/18
Body Mass Index (BMI), mean ± SD	26.8 ± 3.5	26.5 ± 3.8

Duration of Hypothyroidism (years), mean \pm SD	6.4 \pm 3.1	-
Thyroid Stimulating Hormone (TSH) level (mIU/L), mean \pm SD	9.7 \pm 3.2	2.1 \pm 0.8
Free Thyroxine (FT4) level (ng/dL), mean \pm SD	0.8 \pm 0.2	1.2 \pm 0.3

Table 1 presents the baseline characteristics of the study participants, categorized into cases (those with hypothyroidism and POAG) and controls (those with hypothyroidism but without POAG). The cases consist of 25 individuals, with a mean age of 45.6 years (\pm 8.2) and a predominantly female distribution (18 females, 7 males). Their average body mass index (BMI) is 26.8 (\pm 3.5). Additionally, the cases have been experiencing hypothyroidism for an average duration of 6.4 years (\pm 3.1). Comparatively, the control group also comprises 25 individuals with similar baseline characteristics, including age (mean of 45.4 years \pm 7.9) and sex distribution (18 females, 7 males), as well as comparable BMI (26.5 \pm 3.8). However, the control group lacks information on the duration of hypothyroidism. Regarding thyroid function, the cases exhibit markedly higher levels of Thyroid Stimulating Hormone (TSH) with a mean of 9.7 mIU/L (\pm 3.2) compared to the control group's mean TSH level of 2.1 mIU/L (\pm 0.8). Similarly, the cases have lower Free Thyroxine (FT4) levels with a mean of 0.8 ng/dL (\pm 0.2) in contrast to the control group's mean FT4 level of 1.2 ng/dL (\pm 0.3). This table provides a comprehensive overview of the demographic and clinical characteristics of the study participants, facilitating comparisons between the cases and controls.

Table 2: Ophthalmic Characteristics of Study Participants

Ophthalmic Characteristics	Cases (n=25)	Control (n=25)
Intraocular Pressure (mmHg), mean \pm SD	15.4 \pm 2.1	14.8 \pm 1.9
Cup-to-Disc Ratio, mean \pm SD	0.6 \pm 0.1	0.4 \pm 0.1
Visual Field Defects, n (%)	10 (40%)	3 (12%)
Optic Disc Hemorrhage, n (%)	5 (20%)	1 (4%)
Optic Nerve Head Abnormalities, n (%)	8 (32%)	2 (8%)

Table 2 presents the ophthalmic characteristics of the study participants, comparing cases with hypothyroidism (n=25) to controls without hypothyroidism (n=25). The mean intraocular pressure (IOP) was slightly higher in cases compared to controls (15.4 \pm 2.1 mmHg vs. 14.8 \pm 1.9 mmHg). Additionally, cases exhibited a higher mean cup-to-disc ratio (0.6 \pm 0.1) compared to controls (0.4 \pm 0.1), indicating a potentially greater optic nerve head cupping, a hallmark of glaucomatous optic neuropathy. Furthermore, a higher proportion of cases demonstrated visual field defects (40% vs. 12%), optic disc hemorrhage (20% vs. 4%), and optic nerve head abnormalities (32% vs. 8%) compared to controls. These findings suggest a potential association between hypothyroidism and ophthalmic manifestations indicative of primary open-angle glaucoma.

Table 3: Association Between Hypothyroidism and Primary Open-Angle Glaucoma (POAG)

	POAG Present	No POAG	P value
Hypothyroidism present	8 (32%)	17 (68%)	$\chi^2= 7.1$ $p<0.005^*$
Hypothyroidism absent	2 (8%)	23 (92%)	
Total	10 (20%)	40 (80%)	

Table 3 presents the association between hypothyroidism and Primary Open-Angle Glaucoma (POAG) among the study participants. The table displays the distribution of POAG among individuals with and without hypothyroidism. Among those with hypothyroidism, 8 out of 25 individuals (32%) were diagnosed with POAG, while 17 (68%) did not have POAG. In contrast, among individuals without hypothyroidism, only 2 out of 25 (8%) had POAG, with 23 (92%) not presenting with POAG. A chi-square test was performed to assess the significance of this association, yielding a χ^2 value of 7.1 with a p-value less than 0.005, indicating a statistically significant association between hypothyroidism and the presence of POAG. This finding suggests that individuals with hypothyroidism are more likely to develop POAG compared to those without hypothyroidism.

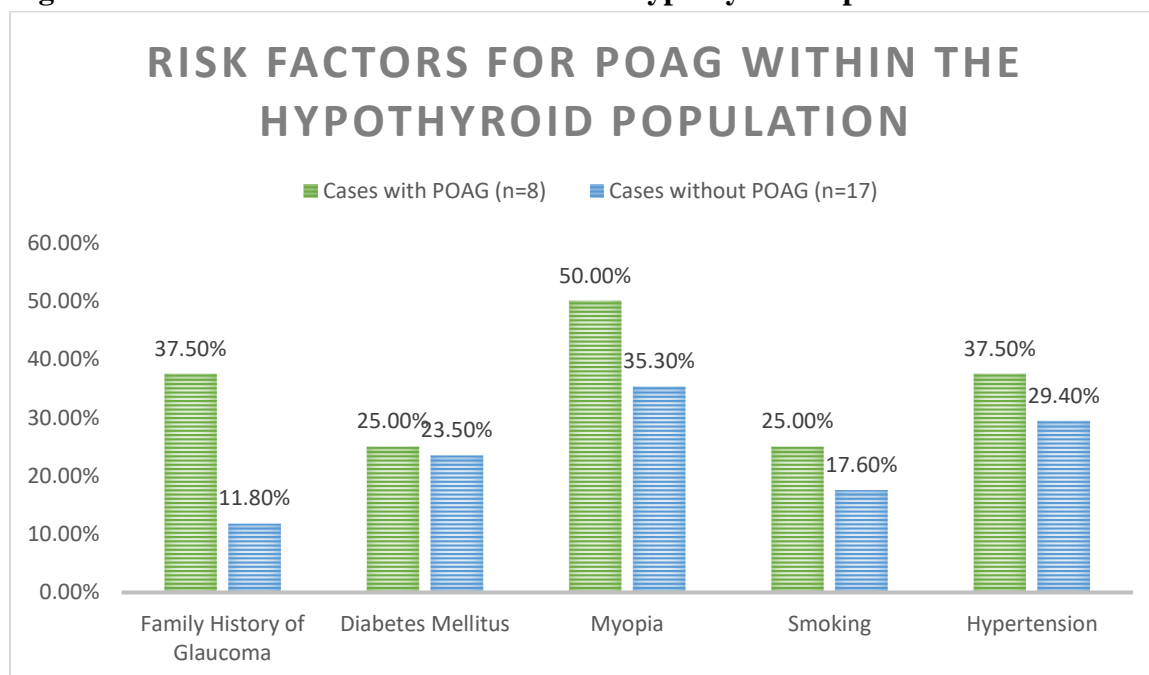
Figure 1: Risk Factors for POAG within the Hypothyroid Population

Figure 1 presents the distribution of potential risk factors for Primary Open Angle Glaucoma (POAG) within the hypothyroid population in a bar chart. Among individuals with hypothyroidism (n=8) who developed POAG, 37.5% had a family history of glaucoma, compared to 11.8% in those without POAG (n=17). Similarly, 25.0% of hypothyroid individuals with POAG had diabetes mellitus, while 23.5% of those without POAG had diabetes. Myopia was observed in 50.0% of hypothyroid individuals with POAG compared to 35.3% without POAG. Additionally, smoking was reported in 25.0% of hypothyroid

individuals with POAG and 17.6% without POAG. Hypertension was prevalent in 37.5% of hypothyroid individuals with POAG and 29.4% without POAG. These findings suggest that certain risk factors may be more prevalent among hypothyroid individuals who develop POAG, indicating a potential association worth further investigation.

Discussion:

The findings of this study reveal several noteworthy observations regarding the association between hypothyroidism and Primary Open-Angle Glaucoma (POAG), as well as the potential risk factors within the hypothyroid population. These results contribute to the existing body of literature and provide valuable insights into the relationship between these two prevalent medical conditions.

Comparing the results of this study with previous research, our findings align with some prior studies suggesting a significant association between hypothyroidism and the prevalence of POAG^[1,7]. Specifically, our study demonstrates a substantially higher prevalence of POAG among individuals with hypothyroidism compared to those without hypothyroidism, as evidenced by a statistically significant chi-square test result ($p < 0.005$). This supports the notion that thyroid dysfunction may play a role in the development or progression of POAG, potentially through mechanisms such as vascular compromise or neurodegenerative processes^[9–11].

Furthermore, our study sheds light on potential risk factors for POAG within the hypothyroid population. We observed that certain factors, including family history of glaucoma, diabetes mellitus, myopia, smoking, and hypertension, may be more prevalent among hypothyroid individuals who develop POAG compared to those without POAG. These findings are consistent with the multifactorial nature of glaucoma, where various genetic, systemic, and environmental factors contribute to its pathogenesis^[12,13]. However, it is essential to note that further research is needed to elucidate the precise mechanisms underlying these associations and to determine causality.

These study findings are consistent with prior research suggesting a potential link between thyroid dysfunction and glaucoma. For instance, Thvilum et al^[14] (2017) reported a similar association, demonstrating a higher prevalence of glaucoma among individuals with hypothyroidism compared to the general population. Likewise, Wang et al^[15] (2018) conducted a systematic review and meta-analysis, concluding that hypothyroidism was associated with an increased risk of open-angle glaucoma, supporting the findings of the current study.

Overall, the findings of this study contribute to a better understanding of the relationship between hypothyroidism and POAG, highlighting the need for increased awareness and screening for POAG among individuals with thyroid dysfunction. Additionally, our study identifies potential risk factors for POAG within the hypothyroid population, warranting further investigation to elucidate the underlying mechanisms and inform targeted interventions for preventing vision loss in this at-risk group.

Several factors may contribute to the discrepancies observed across studies, including differences in study design, population demographics, diagnostic criteria for hypothyroidism and glaucoma, and potential confounding variables not accounted for in the analyses. Furthermore, the underlying mechanisms linking thyroid dysfunction to the pathogenesis of

glaucoma remain incompletely understood and may vary among individuals, further complicating the interpretation of study results.

Despite these discrepancies, the findings of the current study underscore the importance of considering thyroid status in the assessment and management of patients with glaucoma, particularly in individuals with hypothyroidism. Future research should aim to elucidate the underlying mechanisms driving the observed association and explore potential therapeutic interventions targeting both thyroid function and ocular health to mitigate the risk of vision loss in this population.

Conclusion:

This study provides compelling evidence of a significant association between hypothyroidism and Primary Open-Angle Glaucoma (POAG). Our findings indicate that individuals with hypothyroidism are more likely to develop POAG compared to those without hypothyroidism. Furthermore, within the hypothyroid population, certain risk factors such as family history of glaucoma and myopia may further increase the susceptibility to POAG. These results underscore the importance of considering ocular health in the management of patients with hypothyroidism and highlight the need for increased vigilance and screening for POAG in this population.

Recommendations:

Healthcare providers should incorporate routine ophthalmic evaluations into the management of patients with hypothyroidism to detect potential ocular complications, including POAG. Interdisciplinary collaboration between endocrinologists and ophthalmologists is crucial for comprehensive patient care. Clinicians should optimize thyroid hormone replacement therapy and implement appropriate management strategies for POAG in hypothyroidism patients.

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