ORIGINAL RESEARCH ARTICLE

Serum Vitamin D and Uric Acid Levels in Glaucoma Patients: A Comprehensive Investigation

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Abstract

Objective: Glaucoma is an eye condition characterized by optic nerve damage due to inflammation and oxidative stress, often associated with increased intraocular pressure (IOP). Vitamin D, a fat-soluble vitamin with anti-inflammatory properties, and uric acid (UA), an antioxidant molecule capable of scavenging nitrogen radicals and superoxide in plasma, were the specific biomarkers of interest in this research. Therefore, the aim of this study was to assess serum levels of vitamin D and UA in glaucoma patients within the North Indian population.

Materials and methods: The study enrolled 45 age and sex-matched controls and 45 glaucoma patients. Serum levels of vitamin D and UA were measured using the radioimmunoassay (RIA) and enzymatic methods, respectively.

Results: The analysis revealed that the mean of vitamin D in the test group was 23.42 ± 6.56 (ng/mL), while in the control group, it was 29.28 ± 2.58 (ng/mL). Similarly, the UA level was 4.57 ± 1.19 (mg/dL) in the test and 5.87 ± 1.74 in the control.

Conclusion: The present research demonstrated that the level was significantly lowered in both vitamin D and UA in glaucoma patients compared to healthy individuals. These findings emphasize the importance of routinely estimating serum vitamin D and UA in individuals suspected of having glaucoma. Additionally, the results may prove valuable for ophthalmologists in managing and monitoring patients with glaucoma.

Keywords: Glaucoma, Optic nerve, Radioimmunoassay, Uric acid, Vitamin D.

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Introduction

Glaucoma is a prevalent and serious eye condition, affecting more than 70 million individuals globally, with approximately 10% of patients experiencing bilateral blindness. It stands as the leading cause of irreversible blindness worldwide. As the population grows and effective causative treatments remain elusive, the burden of glaucoma continues to increase. Several primary risk factors for glaucoma include higher cup-to-disc ratio, advanced age, central corneal thickness, family history, and elevated intraocular pressure (IOP). Of these factors, IOP stands as a modifiable risk factor, and reducing it has been shown to effectively slow glaucoma progression. Elevated IOP results from an imbalance in the eye's ability to produce and drain the fluid aqueous humor[1–9]

Vitamin D has a crucial role in various biological processes, immune modulation, cellular proliferation encompassing inflammation reduction, glucose metabolism, and oxidative stress regulation. For evaluating vitamin D status in one, 25-hydroxy vitamin-D [25(OH)D] serves as the most consistent biomarker. Notably, vitamin D is involved in regulating neuroprotective functions, including those of the optic nerve, while exerting anti-inflammatory effects by inhibiting T-helper cell and cytotoxic T-cell activation and decreasing the production of interleukin (IL)–2, –6, –8, and –12.

Uric acid (UA), formed primarily in the liver, intestines, and vascular endothelium through purine metabolism, holds significant antioxidant properties, contributing to over half of the antioxidant capacity of blood plasma in humans. Furthermore, UA acts as a major antioxidant, exhibiting metal chelating abilities, scavenging nitrogen radicals and superoxide, and thwarting the generation of strong oxidant peroxynitrite. Consequently, UA is hypothesized to play a protective role in safeguarding the central nervous system against oxidative damage.

Despite the importance of vitamin D and UA in neuroprotection and antioxidant defense, few studies have explored their levels in glaucoma patients. Therefore, the present study aims to assess the serum levels of vitamin D and UA in glaucoma patients, particularly, in the North Indian population. Additionally, this research seeks to establish potential correlations between these serum levels and IOP, providing valuable insights into the pathophysiology and management of glaucoma.

Materials and Methods

This cross-sectional study was carried out in the Department of Biochemistry, Regional Institute of Ophthalmology, Pandit Bhagwat

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Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India. Patients were in the age-group of 40–70 years. This study included 45 patients (cases) with glaucoma reporting in the outpatient department (OPD) of the Regional Institute of Ophthalmology. Age–sex-matched 45 healthy volunteers were taken as controls. The sample size was calculated using a tool (sample size calculator tool from the website, clincalc.com). For calculating the sample size by comparing two means a previous study data (mean) was taken for calculation ($\alpha = 0.05$, $\beta = 0.05$, and power = 0.95).

History was taken from glaucoma patients and all the information was recorded as per pro forma attached. This study was ethically approved by the member secretary, Biomedical Research Ethics Committee PGIMS/UHS Rohtak, Haryana, India (No. BREC/Th/20/BIO/01, dated 2 April 2021), and informed consent was acquired from all participants.

Inclusion Criteria

Patients having any type of glaucoma except glaucoma due to trauma reporting in the OPD of the Regional Institute of Ophthalmology were included in group I.

Exclusion Criteria

Patients with self-reported systemic diseases, including acute infectious diseases, hyperuricemia, diabetes, hypertension, autoimmune disease, metabolic syndrome, kidney disease, and cancer, were excluded from the study.

For biochemical investigations, blood samples were collected *via* venipuncture from the antecubital vein using red-capped vacutainers (6 mL). The radioimmunoassay (RIA) method was used for analyzing the levels of vitamin D present in serum,[10] while serum UA levels were estimated through the enzymatic method on a Randox autoanalyzer.[11]

Statistical Analysis

Statistical analysis was conducted using Microsoft Excel 2019. The Shapiro–Wilk W test was employed to determine the normal distribution of the data. All patient parameters were presented as mean ± standard deviation (SD). If the value of $p < 0.05$, data were believed to be statistically significant; if $p < 0.01$, then highly significant; and the data were insignificant if $p > 0.05$. The unpaired *t*-test (two tailed) was used for statistical tests.

Results

In the study, a total of 45 individuals were detected with glaucoma and 45 age–sex-matched healthy controls were recruited for the investigation. The study cohort comprised 90 participants with ages ranging between 40 and 70 years, who were divided into two groups: cases (glaucoma patients) and controls (apparently healthy individuals). The mean age of the cases was 52.55 ± 8.11 years, and that of the controls was 50.84 ± 8.87 years, with no significant difference between the groups ($p > 0.05$) (Table 1). Additionally, the male-to-female ratio was comparable, and the difference in sex distribution was not statistically significant based on the Chi-square test ($p > 0.05$) (Table 1).

Regarding the serum levels of vitamin D, the mean value for cases was 23.42 ± 6.56 ng/mL, while for controls, it was 29.28 ± 2.58 ng/mL (Table 2). On the bases of the t-test, there was a statistically significant ($p < 0.05$) difference between the Vitamin D levels of the two groups (Table 2).

As for the serum levels of UA, the mean value for cases was 4.57 ± 1.19 mg/dL, and for controls, it was 5.87 ± 1.74 mg/dL (Table 2).

Table 1: Age and gender distribution in both the groups

	Cases		*Controls*		*p-value*
Mean ± SD	52.55 ± 8.11		50.84 ± 8.87		>0.05
Age range	40–70 years		40–70 years		
	Number	*%*	*Number*	*%*	>0.05
Male	24	53.34	23	51.12	
Female	21	46.66	22	48.88	
Total	45	100	45	100	

Table 2: Biochemical parameters in both the groups

Parameters	*Cases*	*Controls*	*p-value*
Vitamin D (ng/mL)			
Mean ± SD	23.42 ± 6.56	29.28 ± 2.58	<0.05
Range	10.8–43.43	24.12–35.95	
UA (mg/dL)			
Mean ± SD	4.57 ± 1.19	5.87 ± 1.74	<0.05
Range	2.9–7.8	3.5–10.1	

Similar to vitamin D, the difference in UA levels between the cases and controls was statistically significant ($p < 0.05$) according to the *t*-test (Table 2).

These findings demonstrate that glaucoma patients have significantly lower levels of both vitamin D and UA compared to healthy individuals. The observed associations between vitamin D, UA, and glaucoma may provide valuable insights into the pathogenesis of the disease and could potentially guide future therapeutic strategies (Table 2).

Conclusion

In this research, we conducted a hospital-based, cross-sectional study with the primary objective of estimating and examining the correlation between serum vitamin D and UA levels with IOP in glaucoma patients. Glaucoma is recognized as a complex and multifactorial eye disorder influenced not only by IOP but also by various systemic conditions. As researchers aim to identify modifiable risk factors beyond IOP, investigations into systemic factors that may contribute to glaucoma development have been undertaken. This study aims to shed light on the potential associations between serum vitamin D, UA levels, and IOP in glaucoma, providing valuable insights into the disease's underlying mechanisms and potential avenues for future interventions.

The mean age was comparable between both groups ($p > 0.05$). The male and female ratio was also comparable. Based on the Chi-square test, this difference in the sex ratio was observed to be statistically insignificant ($p > 0.05$), and comparable which was in accordance with other studies.[6,12–14]

According to the *t*-test, there was a significant difference between the vitamin D levels of the groups ($p < 0.05$). Our research participants were in the age range between 40 and 70 years. It is generally less common to have a deficiency of vitamin D in this age-group compared to those over 60. Factors such as being female, advanced age, less sun exposure, having a dark skin type, and poor dietary habits that lack vitamin D in foods have been linked to its deficiency. Vitamin D levels are influenced by its formation within the skin since dietary intake is often low and the ability to produce Vitamin D weakens with age due to skin thinning.[15] A study conducted in the South Korean population found a result similar

to the current study regarding the association between vitamin D and primary open-angle glaucoma (POAG). The study discovered a reverse J-shaped association, indicating a significantly increased risk of POAG at lower vitamin D levels. This study's findings align with the previous research, suggesting that vitamin D deficiency could be a potential risk factor for POAG development.[12] The reduced amount of vitamin D in the body can lead to the possibility of glaucoma development. Vitamin D has the potential to provide protection through various means, such as activating the vitamin D receptor or regulating calcium balance.[16] It can also impact immune cell functions, which could help in safeguarding the optic nerve.[17] Vitamin D plays a crucial role in regulating oxidative stress on neurons through the activation of calcium channels.[18] Extensive research over the past two decades has pointed to the close association of vitamin D with various neurodegenerative and psychiatric disorders.[19] Moreover, vitamin D exhibits an anti-inflammatory effect, countering endothelial dysfunction caused by metabolic damage or oxidative stress.[20] The emerging understanding of these new mechanisms is opening intriguing possibilities in the management of glaucoma, as different patients may experience glaucomatous degeneration through distinct pathways.[21]

In our study, the *t*-test demonstrated a significant difference in UA levels between the groups ($p < 0.05$). Glaucoma patients exhibited lower UA levels compared to healthy individuals, and this negative association with glaucoma aligns with findings from prior research. Previous studies on primary angle-closure glaucoma (PACG) also reported significantly lower mean serum UA and Uric acid to creatinine ratio (UA/Cr) in PACG patients compared to controls ($p < 0.001$), with serum UA levels negatively associated with PACG severity. These observations suggest a potential link between UA, glaucoma development, and oxidative stress in the pathogenesis of PACG.[22–24]

Clinical Significance

The study's clinical significance indicates that lower levels of vitamin D and UA can be a potential risk factor for the development of glaucoma. The data analysis showed that mean serum vitamin D and UA levels were lower in glaucoma cases than in control subjects. This difference was statistically significant ($p < 0.05$). Moreover, individuals with glaucoma exhibited notably lower average serum Vitamin D levels compared to the control group, along with a higher incidence of vitamin D insufficiency. The study also found that mean serum UA levels were decreased and negatively associated with glaucoma. The observed correlation between UA and glaucoma development implies a potential role of oxidative stress in the pathogenesis of the condition. Therefore, it is recommended that serum vitamin D and UA levels should be routinely estimated in all glaucoma suspects, and this study may help ophthalmologists manage and follow up with their glaucoma patients.

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