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Original Article

The Relativity between Vitamin D and Glaucoma - A Cross Sectional Study from Rewa (M.P)

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ABSTRACT

Glaucoma is a chronic progressive optic neuropathy that causes irreversible damage. Therefore, early diagnosis and appropriate treatment to control various risk factors associated with glaucoma are important. Risk factors associated with the development of glaucoma have been reported by many researchers and include both ocular and non-ocular (systemic) factors such as myopia, central corneal thickness, disc hemorrhage, and genetic factors. However, little is known about the association between vitamin D and open-angle glaucoma (OAG). As a consequence, many glaucoma patients are diagnosed, monitored, and treated at an age amply beyond the age corresponding to their median life expectancy at birth. To make a proper estimate of the life expectancy of glaucoma patients, life expectancy should be adjusted for the age already reached: residual life expectancy.

Key words: Optic Neuropathy, Ocular, Myopia, OAG, Median Life, Life Expectancy

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INTRODUCTION

Glaucoma accounts for approximately 8% of global blindness according to the 2010 World Health Organization report. It is the second leading cause of blindness in the world after cataracts, and the leading cause of irreversible loss of vision (1). Despite the huge patient population and severe consequences, the exact etiology of glaucoma is still unclear. Based on glaucoma clinical trials, the established risk factors for glaucoma include older age, intraocularpressure, race, myopia, optic nerve susceptibility, and positive family history (2). Other clinical risk factors, such has various systemic diseases (e.g., diabetes, hypertension, is chemicvascular diseases) and unhealthy behaviours (e.g., smoking, alcohol consumption), remain inconsistent among different studies (3,4). Although there is a large population burden and severe consequence to quality of life, there is a gap in knowledge to advance our understanding beyond the established clinical risk factors for glaucoma .In addition to clinical risk factors, genetic risk factors for glaucoma have been established through the Mendelian studies and genome-wide association studies (GWAS) (5). Adult-onset glaucoma occurs mainly among individuals >40 y of age. Primary open-angle glaucoma (POAG) is the major form of adult-onset glaucoma in the United States (prevalence: 1.9%) (6).

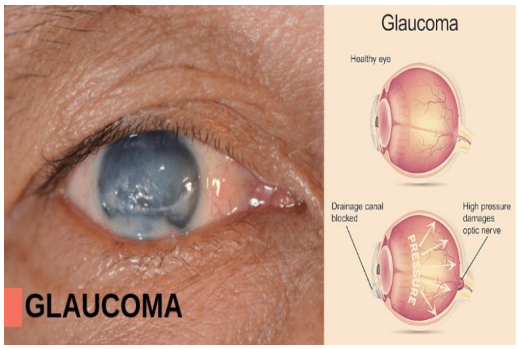
Glaucoma is a multi-factorial optic neuropathy characterized by acquired loss of optic nerve fibres. Cur-rent hypotheses on the potential pathogenic mechanisms in the onset of glaucomatous optic neuropathy include exotoxic lesion due to excessive retinal glutamate release, reduction in neuronal growth factor, per-oxynitrite toxicity due to the increased activity of nitric monoxide synthetase, immune mediated optic nerve lesion, and oxidative stress. There are no generally accepted guidelines on adequate vitamin D (1,25(OH)2D3) level. Serum vitamin D levels of 50-75 nmol/L (20-30 ng/mL) are considered as vitamin D insufficiency, with adverse effects on bone mineral density and possibly on muscle and physical ability (7).

The levels <50 nmol/L are considered as vitamin D deficiency and those <30 nmol/L as severe vitamin D deficiency, whereas vitamin D levels <20 nmol/L cause serious impairment of bone metabolism, i.e. rickets or osteomalacia, depending on age, as well as myopathy associated with physical inability (8). As a steroid hormone, vitamin D directly or indirectly regulates 3% of the human genome function. Favorable vitamin D effects have been demon-strated in many diseases, e.g., in the prevention of heart attack and stroke, diabetes mellitus type 1 and 2, infections and chronic respiratory diseases, autoim-mune diseases, etc. Vitamin D receptor (VDR) has been found in some ganglion layer cells, external and internal nuclear layers of retina, and in retinal pigment epithelium, though VDR epitopes have also been found in the ciliary body epithelium, pointing to the role of this protein in eye physiology. Vitamin D exerts auto-crine and paracrine action via VDR((9). The mechanism by which vitamin D reduces intraocular pressure (IOP) has not yet been fully clarified. The 1,25(OH)2D3 modulates expression of the genes involved in IOP regulation in non-human primates. Extracellular matrix can be remodeled by 1,25(OH)2D3 treatment, resulting in increased fluid flow along with reduced flow resistance by disruption of cellular adhesions and relaxation of contractile molecules(10). Nitric oxide (NO), a free radical produced by vascular endothelium induced by the endothelial nitric monoxide synthetase (eNOS) enzyme activity, is the important signaling molecule for local regulation of vascular tone. Some studies showed that increased NO levels increased the flow rate and thus reduced IOP(11), whereas others report that the increased NO level led to peroxynitrite toxicity and development of glaucomatous optic neuropathy. The 1,25(OH)2D3 inhibits nitric oxide inducible synthetase (iNOS) expression and reduces NO production in stimulated macrophages. The macrophage production of 1,25(OH)2D3 has protective effect on oxidative lesion caused by NO burst(12).

A sufficient vitamin D status is related with a minor risk of rheumatoid arthritis, multiple sclerosis, diabetes mellitus type 1, autoimmune diseases and neurodegenerative diseases such as glaucoma. Despite the growing knowledge about the biological and clinical role of vitamin D, considerable occurrence of vitamin D deficiency is re-ported in the populations all over the world, with Croatia(13). In common, 25-hydroxyvitamin D (25(OH)D) is believed the mainly reliable biomarker for assessing an individual's vitamin D status. Based on the consequences of serum 25(OH)D measurements in huge population-based studies, vitamin D deficiency is associated with neurodegenerative effects on the central nervous system.

Some biological experiments have indicated that vitamin D controls neuroprotective functions in the central nervous system, including the optic nerve (14) .Studies focusing on vitamin D status and its link to glaucoma are limited and inconsistent .The intention of this study was to investigate the association between vitamin D and the development of glaucoma (15). The aim of this study was to investigate the relativity between vitamin D and glaucoma.

Picture :- The view of Glaucoma .



SIGNS AND SYMPTOMS

Open-angle glaucoma is painless and does not have severe attacks, thus the lack of clear symptoms make screening via regular eye check-ups important. The only signs are regularly progressive visual field loss, and optic nerve changes (increased cup-to-disc ratio on fundoscopic examination). About 10% of people with closed angles present with acute angle closure characterized by rapid ocular pain, seeing halos around lights, red eye, extremely high intraocular pressure (>30 mmHg), nausea and vomiting, suddenly decreased vision, and a fixed, mid-dilated pupil. It is also related with an oval pupil in several cases. Acute angle closure is an emergency. Opaque specks may arise in the lens in glaucoma, known as glaukomflecken(16).

TYPES OF GLAUCOMA

There are several types of glaucoma. The two main types are open-angle and angle-closure. These are marked by an increase of intraocular pressure (IOP), or pressure inside the eye.

Open-Angle Glaucoma

Open-angle glaucoma, the mainly common form of glaucoma, accounting for at least 90% of all glaucoma cases:

- Is caused by the slow clogging of the drainage canals, resulting in increased eye pressure
- Has a wide and open angle between the iris and cornea
- Develops slowly and is a lifelong condition
- Has symptoms and damage that are not noticed.

“Open-angle” means that the angle where the iris meets the cornea is as wide and open as it should be. Open-angle glaucoma is also called primary or chronic glaucoma. It is the largely common type of glaucoma .

Angle-Closure Glaucoma

Angle-closure glaucoma, a less common form of glaucoma:

- Is caused by blocked drainage canals, resulting in a sudden rise in intraocular pressure
- Has a closed or narrow angle between the iris and cornea
- Develops very quickly
- Has symptoms and damage that are usually very noticeable
- Demands immediate medical attention.

It is also called acute glaucoma or narrow-angle glaucoma. Unlike open-angle glaucoma, angle-closure glaucoma is a result of the angle between the iris and cornea closing.

Normal-Tension Glaucoma (NTG)

Also called low-tension or normal-pressure glaucoma. In normal-tension glaucoma the optic nerve is damaged even though the eye pressure is not very high. We still don't know why some people’s optic nerves are damaged even though they have almost usual pressure levels.

Congenital Glaucoma

This type of glaucoma occurs in babies when there is incorrect or incomplete development of the eye's drainage canals during the prenatal period. This is a rare condition that may be inherited. When uncomplicated, microsurgery can often correct the structural defects. Other cases are treated with medication and surgery.

Other Types of Glaucoma

Variants of open-angle and angle-closure glaucoma include:

- Secondary Glaucoma
- Pigmentary Glaucoma
- Pseudoexfoliative Glaucoma
- Traumatic Glaucoma
- Neovascular Glaucoma
- Irido Corneal Endothelial Syndrome (ICE)
- Uveitic Glaucoma (17)

MATERIALS AND METHODS

This study followed the principles of the Declaration of Hel-sinki. Subjects who underwent health screening at one of the APS University screening centers in Rewa from August 2019 to March 2020 were enrolled in this retrospective, cross-sectional study. The intention of the screening program was to encourage health through early detection of chronic diseases and their risk factors. Additionally, the Indian Industrial Safety and Health Law requires working individuals to participate in an annual or biennial health examination. About 60% of the participants were employees (or their spouses) of companies or local governmental organizations, while the remaining participants registered individually for the program. During the screening test, digital color fundus photographs were taken with a digital fundus camera (CR6-45NM; Canon, Tokyo, Japan). The

IOP was determined using a noncontact tonometer (CT-80; Topcon, Tokyo, Japan), and the mean value of two IOP readings was recorded. In addition to fundus photographs, systemic examination and socio-demographic and behavioral questionnaires were administered to all subjects; their medical histories were also checked to determine the presence of any associated systemic disease. All fundus photographs were checked by two ophthalmologists, two glaucoma specialists, and one retinal specialist, all of whom were blinded to the subjects' demographic features and laboratory findings. Discrepancies among the observers' findings were resolved by consensus. Fundus photographs were divided into two groups based on disc and retinal nerve fiber layer (RNFL) appearance: non-glaucoma and glaucoma, described as glaucomatous optic disc diagnosed according to International Society of Geographical and Epidemiological Ophthalmology (IS-GEO) criteria or definite RNFL defect. A glaucomatous optic disc was described based on disc appearance such as disc notching or cup-to-disc ratio (CDR) superior than 0.7 vertical CDR or superior than 0.2 vertical CDR asymmetry between the right and left eyes. A glaucomatous RNFL defect was described as a localized, wedge-shaped RNFL defect within 60 degrees of the optic disc border. In cases with newly-detected glaucomatous features, glaucoma evaluations were suggested for confirmation, and a few subjects were diagnosed with glaucoma after under-going a glaucoma evaluation in the glaucoma clinic. The subjects diagnosed with glaucoma in the glaucoma clinic were enrolled as the glaucoma group. Non-glaucomatous RNFL defects, such as better segmental optic hypoplasia, slit defects, and spindle-like defects, were excluded. The following variables were examined to evaluate the risk factors of improvement of glaucoma: physical measurements (body mass index, waist circumference, and systolic and diastolic blood pressure), serum biochemical measurements (fasting blood glucose, hemoglobin A1c, and serum 25(OH)D), serum lipid profiles (total cholesterol and triglycerides), medical history (presence of diabetes, systemic hypertension, hyperlipidemia, hyperthyroidism, or hypothyroidism), and a questionnaire that addressed socio demographic characteristics (age and sex) and health-related behaviours (smoking, alcohol intake, and physical activity). Alcohol intake was categorized based on a cut-off of 20 g/day. In addition, usual physical activity was based on moderate levels of physical activity, such as carrying light loads, bicycling, or doubles tennis (18).

Statistics: Analyses were executed with Statistical Package for the Prism version 2.0. Each variable was initially evaluated by the chi-square test or independent t-test. After adjusting for confounding variables such as sex, age, current smoking, diabetes, hypertension, and IOP, multivariate linear regression analysis was used to analyze the association between developing glaucoma and vitamin D or developing glaucoma and quintile of vitamin D. Model 1 was not adjusted; model 2 was adjusted for age, sex, cur-rent smoking status, diabetes, and hypertension; model 3 was adjusted for age, sex, current smoking status, diabetes, hypertension, and IOP. Odds ratios (ORs) with 95% confidence intervals were produced using a linear regression model. Additionally, the glaucoma group was separated into high IOP and without high IOP groups based o n 21 m m Hg IOP, and the difference in vitamin D levels between the two groups was analyzed using independent t-test. A p-value <0.05 was considered statistically significant.

OBSERVATION

The present study entitled - The Relativity between Vitamin D and Glaucoma - A Cross Sectional Study from Rewa **(**M.P) was undertaken in the department of Biochemistry APS University REWA (M.P) .From August 2019 to March 2020. A total of 2000 subjects were enrolled in the present study following were the observations.

Table 1: Demographic and general health characteristics of the study subjects

Characteristics	Glaucoma(+)(1272)	Glaucoma (-)(1724)	p-value
Age (yr)	42.16 ±0.01673	39.46 ±0.03203	P<0.0001*
Male	548 (43%)	724 (42%)	P = O. 1818†
IOP (mmHg)	15.33 ±0.1030	14.33 ± 0.5625	P<0.0001*
Systolic BP (mmHg)	110.4 ± 0.09067	106.9 ± 0.09149	P<0.0001*
Diastolic BP (mmHg)	72.71 ± 0.1143	69.74 ± 0.6211	P<0.0001*
Pulse pressure (mmHg)	37.75 ± 0.003033	37.13 ± 0.003469	P<0.0001*
FBS (mg/dL)	97.77 ±0.002105	94.88 ± 0.1590	P<0.0001*
Hemoglobin A1c (%)	5.662 ± 0.02107	5.602 ± 0.1984	P<0.0001*
Total cholesterol (mg/dL)	198.3 ± 0.002339	195.7 ± 0.01105	P<0.0001*
Triglycerides (mg/dL)	126.3 ± 0.01725	113.2 ± 0.002448	P<0.0001*

BMI (kg/m2)	23.76 ±0.02488	23.32 ± 0.005529	P<0.0001*
Waist circumference (cm)	84.02 ± 0.01162	81.85 ± 0.1764	P<0.0001*
Total vitamin D (ng/dL)	15.85 ± 0.01589	16.49 ± 0.2335	P<0.0001*
Diabetes	80 (6.2)	210 (12.1)	P<0.0001†
Hypertension	130 (10.2)	200 (12)	0.2849†
Hyperlipidemia	162 /1107 (15)	215 /1620 (13.2)	0.3789†
Current smoker	224 /800 (28)	230/1650 (14)	P<0.0001†
Alcohol drinker	160/1150 (14.1)	190/1636 (11.6)	0.1127†
Regular exerciser	200 /1220 (16.3)	250/1540 (16.2)	0.9238†
Hyperthyroidism	171 /840 (20.3)	260 /1280 (20.3)	0.9838†
Hypothyroidism	145 /1000 (14.5)	169/1250 (13.52)	0.6042†

Values are presented as mean ± standard deviation or number (%).IOP = intraocular pressure; BP = blood pressure; FBS = fasting blood glucose; BMI = body mass index.*Student's t-test; †Chi-square test.

Table 2: Prevalence of glaucoma according to quintile of serum 25(OH)D .

	Serum 25(OH)D level quintile					
	1st quintile (≤10.06)	2nd quintile (10.07-13.10)	3rd quintile (13.11-16.36)	4th quintile (16.37-21.00)	5th quintile (≥21.01)	P-value
Total	265/370 (71.6%)	280/300(93.33%)	315/375 (84%)	340/460 (74%)	72/219 (33%)	P<0.0001*
Male	104/150 (69.3%)	126/135 (93.33%)	148/152 (97.3%)	140/160 (87.5%)	30/80 (37.5%)	P=0.0007*
Female	161/220 (73.18%)	154/165 (93.3%)	167/223 (75%)	200/300 (66.6%)	42/139(32.2%)	P<0.0001*

25(OH)D = 25-hydroxyvitamin D. *Chi-square test.

Graph - Numbers of Male and Female glaucoma Patients according to the Age Groups .

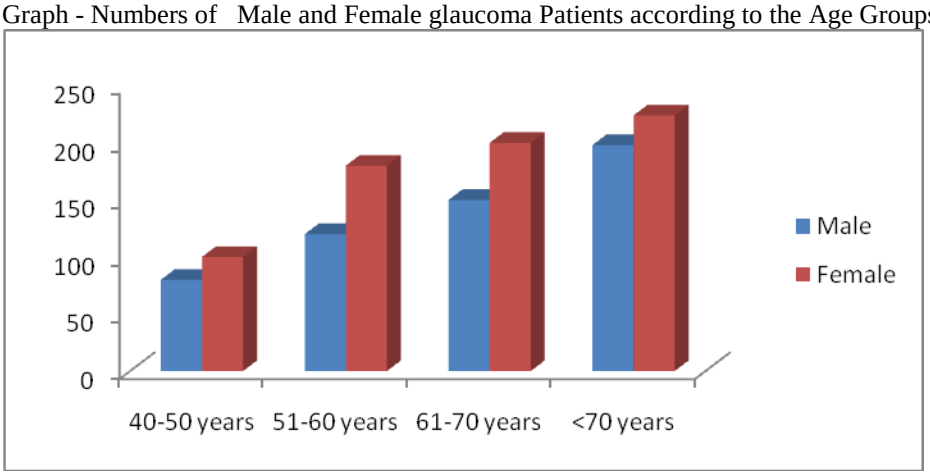


Table-3 ORs of glaucoma according to quintile of serum 25(OH)D in all subjects .

	Serum 25(OH)D level quintile							
	1st quintile (≤10.06)	2nd quintile (10.07-13.10)	3rd quintile (13.11-16.36)	4th quintile (16.37-21.00	5th quintile (≥21.01)	P value For linear trend	Change in OR for a 1 ng/dL increase in 25(OH)D	
	OR	OR (95% CI)					OR	p-value
Total								
Model 1	1.00 (ref)	1.060 (0.776-1.448)	1.271 (0.8581-1.883)	1.030 (0.7005-1.515)	0.8605 (0.5768-1.284)	P<0.0001*	1.130	P<0.0001*

Model 2	1.00 (ref)	1.005 (0.6575-1.537)	1.346 (0.8704-2.080)	0.8581 (0.5634 - 1.307)	0.9048 (0.6100-1.342)	P<0.0001*	1.003	P<0.0001*
Model 3	1.00 (ref)	0.8983 (0.6163-1.309)	0.9829 (0.6563-1.472)	1.041 (0.6891-1.572)	0.9634 (0.6651-1.395)	P<0.0001*	0.7975	P<0.0001*
Male								
Model 1	1.00 (ref)	1.435 (0.7754 - 2.657)	0.9651 (0.5110-1.809)	1.472 (0.7758-2.793)	0.6591 (0.3540-1.227)	P=0.0007*	0.8429	P=0.0006*
Model 2	1.00 (ref)	1.067 (0.5354-2.128)	0.9300 (0.4755-1.819)	0.8995 (0.4909-1.648)	1.307 (0.6357-2.686)	P<0.0001*	0.9600	P=0.0011*
Model 3	1.00 (ref)	1 (0.5617-1.780)	1.333 (0.7113-2.499)	0.7337 (0.3993-1.348)	1.001 (0.5865-1.710)	P<0.0001*	1.162	P<0.0001*
Female								
Model 1	1.00 (ref)	0.8955 (0.5130-1.563)	0.9778 (0.5513-1.734)	1.26 (0.7539-2.116)	0.9218 (0.5665-1.500)	P<0.0001*	0.9584	P<0.0001*
Model 2	1.00 (ref)	1.216 (0.6322-2.339)	0.9309 (0.4999-1.733)	1.074 (0.6642-1.792)	0.9375 (0.5497-1.599)	P<0.0001*	1.113	P<0.0001*
Model 3	1.00 (ref)	1.197 (0.6842-2.095)	0.7692 (0.4300-1.376)	0.8989 (0.5589-1.446)	1.280 (0.8224-1.993)	P<0.0001*	0.9644	P<0.0001*

Model 1 was not adjusted; Model 2 was adjusted for age, sex, current smoking status, diabetes, and hypertension; Model 3 was adjusted for age, sex, current smoking status, diabetes, hypertension, and intraocular pressure. OR = odds ratio; 25(OH)D = 25-hydroxyvitamin D; CI = confidence interval. *linear regression analysis

RESULTS

Subject characteristics according to the presence or absence of glaucoma are shown in Table 1. A total of 2000 subjects were enrolled in the present study. Among the eligible subjects, 1272 had glaucoma. The glaucoma group consisted of 750 subjects who were diagnosed in the glaucoma clinic based on a standard glaucoma evaluation and 526 who were diagnosed using ISGEO criteria and had RNFL defects. The following variables were all statistically different between the glaucoma and the healthy groups: age; percentage of males; IOP; systolic and diastolic blood pressure; pulse pressure; fasting blood glucose; hemoglobin A1c; total cholesterol; triglycerides; body mass index; waist circumference; serum 25(OH)D; presence of diabetes, , hypertension, hyperlipidemia; and current smoking status. However, alcohol intake, regular exercise, and presence of hyperthyroidism and hypothyroidism were not statistically significantly different between the two groups. The prevalence of glaucoma, according to quintile of serum 25(OH)D is shown in Table 2. The prevalence of glaucoma was statistically significantly different between various 25(OH)D quintiles ($p < 0.0001$); however, after adjusting for sex, the prevalence of glaucoma was statistically significantly different between the 25(OH)D quintiles. The ORs of glaucoma according to serum 25(OH)D and serum 25(OH)D quintiles are shown in Table 3 linear regression analysis showed that the ORs for subjects in the third, and fourth, quintiles of serum 25(OH)D were significantly higher than the ORs for first quintile subjects (OR s , 1.271, and 1.030, respectively; P< 0.0001). When the linear regression analyses were conducted using continuous serum 25(OH)D level, the OR of glaucoma for every 1 ng/dL increase in 25(OH)D was significantly changed (OR, 1.130). In linear regression analysis according to sex, continuous value or quintile of serum 25(OH)D was not significantly associated with glaucoma in males. However, in females, the OR of subjects in the fourth quintile of serum 25(OH)D was significantly higher than that in the first quintile subjects (OR, 1.26)

DISCUSSION

Glaucoma is considered a complex and multi-factorial disorder that is influenced not only by IOP, but also different systemic conditions. To recognize controllable risk factors other than IOP, several researchers have investigated the systemic factors that affect the development of glaucoma. Some mechanisms underlying this association remain unclear. According to my study Table- 1

showed general health characteristics like IOP, Systolic BP, Diastolic BP , Pulse pressure, FBS Hemoglobin A1c , was significantly different between Glaucoma patients and non Glaucoma patients .This study similar to the study of (18). Potential mechanisms for the development of glaucoma might be influenced by several protective roles of vitamin D, either directly by activation of the vitamin D receptor or indirectly by regulation of calcium homeostasis. First, vitamin D might affect immune-modulation in the pathogenesis of glaucoma (19). According to my study Table-2 shown the prevalence of glaucoma according to quintile of serum 25(OH) D. The prevalence of glaucoma was statistically significantly different between various 25(OH)D quintiles ($p < 0.0001$); however, after adjusting for sex, the prevalence of glaucoma was statistically significantly different between the 25(OH)D quintiles. This study is similar to the study of (18). Latest studies have shown that an imbalance of the immune system is a major contributor to neurodegenerative injuries of the optic nerve axons and ganglion cell bodies. While vitamin D significantly affects the regulation of immune cell functions, this effect might play a key role in defending the optic nerve. Second, vitamin D controls both neurotrophic factors in the central nervous system and plasticity in neural net-works (20). According to my study Table- 3 showed, the association between either 25(OH)D or quintile of 25(OH)D and the development of glaucoma was not statistically significant in males. Though, in females, these associations showed statistically significant outcomes. Females with lower 25(OH)D level were at a significantly larger risk of glaucoma compared with those with higher 25(OH)D level . This observation similar to the study of (18). Serum vitamin D was related with IOP in male subjects, and that low vitamin D level in glaucoma subjects might outcome from low external activity due to the disease. This outcome is in contrast with my findings. In my study, there was no relationship between vitamin D status and the development of glaucoma in all subjects or in males. The cause for this difference is unknown. It may be that there were extra female than male subjects in my study, while the previous study population had a different composition. Furthermore, our subjects were enrolled from health-screening canters (21). Therefore, my study was not population-based. Another opportunity is that the subjects in my study were in a higher socioeconomic class and had a more invested interest in their health. Whatever the cause, the association between vitamin D status and glaucoma remains unclear, and further studies are essential. My study showed different outcomes after adjusting for sex. One cause for this difference might be due to the effects of female sex hormones. Female sex hormones were related with glaucoma. An altered sexual hormone status has been shown to lead to nutrition deficiency and various chronic diseases (22). According to some studies, vitamin D status influences female reproductive and pregnancy results, and low vitamin D status is associated with impaired fertility, endometriosis, and polycystic ovary syndrome (23). Based on different studies, vitamin D levels have an influence on the health of females. My study has some limitations. First, the chosen individuals enrolled retrospectively in a health screening program; therefore, the study population was biased to individuals with access to health care. All subjects were self-selected for health screening, and most of the study population consisted of workers and their spouses. The educational and economic demographics of the study subjects might have resulted in some bias. However, my study population was very large, which is expected to minimize selection bias. A future longitudinal study is required.

Second, some subjects were detected with glaucoma based only on fundus photographs. However, most subjects showed RNFL defects in their fundus photographs. To exclude the possibility of misdiagnosis, each examiner diagnosed the fundus photo-graph blindly, and any discrepancies among the observers were resolved by consensus. Third, we could not exactly distinguish the type of glaucoma because we did not perform slit-lamp test in several subjects who were analysed using ISGEO criteria and had RNFL defect. Instead of examination according to the type of glaucoma, we only analyzed the difference in vitamin D level in the subtypes of glaucoma based on IOP. After dividing the glaucoma group based on IOP, serum 25(OH)D levels were not significantly different between the high IOP and with-out high IOP groups. One of the reasons might be the significant difference in the number of subjects in the two groups. Most of the subjects were in the without high IOP group. Fourth, ocular parameters such as axial length, corneal thickness and refractive error were not measured. Fifth, this was a cross-sectional, case-control study; therefore, no causal relationship between development of glaucoma and serum 25(OH)D level could be determine .

CONCLUSION

Glaucoma is a multifactorial optic neuropathy characterized by acquired loss of optic nerve fibers. Lesser serum 25(OH)D level was significantly associated with an elevated risk of glaucoma in women compared to those with higher serum 25(OH)D. My results propose that vitamin D status independently affects the pathophysiology of glaucoma in women. I cannot explain the accurate

mechanism; however, considering both the results of previous reports and the present study, vitamin D influences the pathophysiology of glaucoma as a secondary aggravating factor rather than a primary reason. With the presence of a primary factor, a low vitamin D level might render the optic nerve or its environment extra vulnerable to glaucomatous insult. My study helps to elucidate the risk factors of glaucoma and to disclose the mechanisms underlying the influence of vitamin D on the improvement of glaucoma. If this study results be confirmed, then vitamin D may be considered a marker in the early diagnosis and prevention of glaucoma.

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