• Investigation •

Relationship between intraocular pressure and parameters of obesity in ocular hypertension

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Received: 2019-06-17 Accepted: 2020-02-19

Abstract

● **AIM:** To evaluate the correlation between intraocular pressure (IOP) and various obesity-related health factors in patients with ocular hypertension in Korea.

● **METHODS:** A total of 40 850 subjects underwent age, sex, body weight, and height assessments and automated multiphasic tests, including non-contact tonometry, automated perimetry, fundus photography, systolic/diastolic blood pressure measurement, and evaluation of obesity-related health parameters such as obesity index, body mass index (BMI), a body shape index (ABSI), and waist-to-height ratio (WtHR). Subjects were divided into ocular hypertension group and normal IOP group according to IOP after matching of age and sex.

● **RESULTS:** Of 40 850 participants, 1515 (3.7%) had ocular hypertension, and 1515 with normal IOP were selected as controls using propensity score matching. The mean IOP of control group was 15.3±2.3 mm Hg, compared with 23.3±1.6 mm Hg in ocular hypertension group. Height, obesity index, BMI, and WtHR in the ocular hypertension group were significantly higher than in the normal IOP group (P<0.001, P<0.001, P=0.009, P=0.002). IOP of ocular hypertension was positively correlated with obesity index (P=0.027) and BMI (P=0.016), whereas IOP of control was positively correlated with blood pressure (P<0.001, P=0.002), obesity index (P<0.001), BMI (P<0.001), and WHtR (P=0.002). Systolic blood pressure (β=0.022, P<0.001) and body weight (β=0.016, P=0.02) were precursors of IOP in normal subjects, but sex (male; β=-0.231, P=0.008) and obesity index (β=-0.007, P=0.017) were precursors of ocular hypertension according to multiple regression analysis .

● **CONCLUSION:** Among various obesity-related health parameters, obesity index is the best indicator for further increase in IOP in ocular hypertension group.

● **KEYWORDS:** intraocular pressure; ocular hypertension; body mass index; body shape index; waist-to-height ratio

DOI:10.18240/ijo.2020.05.15

Citation: Ahn MW, Lee JW, Shin JH, Lee JS. Relationship between intraocular pressure and parameters of obesity in ocular hypertension. *Int J Ophthalmol* 2020;13(5):794-800

INTRODUCTION

Glaucoma occurs due to optic neuropathy, resulting in damage to the optic nerve and visual field defects, eventually inducing visual blindness[1-2]. To prevent blindness caused by high intraocular pressure (IOP), early diagnosis of glaucoma and proper treatment for maintaining IOP are needed. Although there are many systemic health factors related to glaucoma pathogenesis, the most well-known factor is IOP. Epidemiological studies have attempted to identify a relationship between IOP and systemic health factors, and current studies are examining the important role of measuring IOP during the early diagnosis and progression of glaucoma.

Ocular hypertension, which is diagnosed in patients with IOP greater than 21 mm Hg without signs of a glaucomatous field or damage to the optic disc, is an important risk factor in glaucoma pathogenesis[3-4]. Some reports show that high IOP is correlated with risk factors including cardiovascular disease, and metabolic syndromes such as obesity, hypertension, hyperglycemia, and hyperlipidemia[5-7]. Many epidemiological studies have examined the systemic risk factors of glaucoma, especially the relationship between IOP and obesity-related health parameters such as body mass index (BMI) and obesity index[8-10]. However, there have been some problems regarding the clinical significance of BMI or the obesity index and the effect on IOP. For example, the indexes cannot differentiate muscle and fat. Thus, new epidemiological studies on obesity-related factors such as body shape index (ABSI) and waist-to-height ratio (WtHR), and their correlation with IOP, are in the limelight.

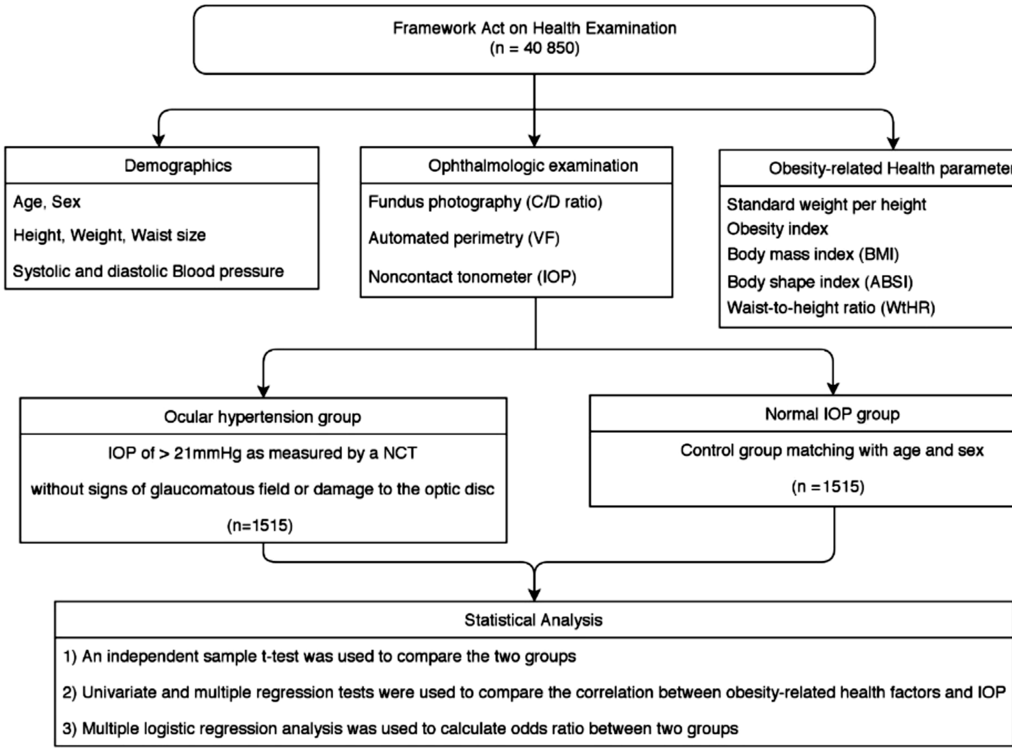

Figure 1 The flow chart of this study.

Whereas most epidemiological studies have shown that subjects either have normal IOP, or they are diagnosed with glaucoma, some epidemiological studies that focus on ocular hypertension and its relationship with obesity-related parameters are very rare. In this study, we are going to compare ocular hypertension with normal IOP to evaluate the correlation between IOP and obesity-related factors, especially ocular hypertension.

SUBJECTS AND METHODS

Ethical Approval The present study protocol was reviewed and approved by the Institutional Review Board of Pusan National University College of Medicine. Informed consent was obtained from the subjects.

We examined 40 850 healthy participants (range 20-84y) at the Health Promotion Center in Pusan National University Hospital. Most subjects were office workers and their family members who resided in the city of Busan (3.5 million residents). The participation rate was approximately 0.05% of the total population of Busan aged 20y or older. We divided participants into 4 age groups by decade, ranging from <40 years to >60 years of age. Before testing, each participant was interviewed about previous health problems and medical history, including ocular disease, by a physician and an ophthalmologist. We excluded subjects with ocular examination results suggestive of any abnormality in at least one eye. The exclusion criteria were as follows: past history of intraocular disease or surgery, or medical treatment for hyperlipidemia, hypertension, and/or diabetes mellitus (Figure 1). The relationship between obesity-related factors and ocular hypertension was analyzed except subjects who were under treatment for metabolic syndrome because such treatment and diabetes may affect IOP and obesity-related factors.

Medical records of 40 850 people were analyzed retrospectively. Blood pressure, height, weight, waist size, standard weight per height, obesity index, BMI, ABSI, and WtHR of patients who visited our medical health center for ocular checkups were measured. Blood pressure was measured using an oscillometric tonometer (Dinamap 8100T, Critikon Inc., Tampa, FL, USA) which had an arm thickness of two-thirds. The mean of 2 systolic and diastolic blood pressure (SBP and DBP) readings was used as the measurement value. Height and weight were measured with subjects wearing a lightweight hospital gown in a standing position without shoes. Waist size was measured at the end of the subject's exhalation, directly above the highest point of the iliac crest.

Standard weight per height was calculated by the formula

$$[(\text{measured height} - 100) \times 0.9] \quad (1)$$

The obesity index was determined by the formula

$$\{[\text{measured weight (kg)}/\text{standard weight per height (kg)}] \times 100\} \quad (2)$$

BMI was determined by the formula

$$[\text{weight (kg)}/\text{height (m}^2)] \quad (3)$$

ABSI was measured according to the formula

$$[\text{waist size (cm)}/\text{BMI}^{2/3} \times \text{height}^{1/2} \text{ (cm)}] \quad (4)$$

WtHR was determined by the formula

$$[\text{waist size (cm)}/\text{height (cm)}] \quad (5)$$

Fundus examination was conducted using an ophthalmoscope (TRC-NW5S, Topcon Corp., Tokyo, Japan), taking 30°

color stereophotographs that included the optic nerve and macula. The IOP was measured by a noncontact tonometer (CT-80, Topcon Corp.), using the median value of 3 identical measurements. To minimize diurnal variation, IOP was measured only between 9:00 a.m. and 11:00 a.m., Monday through Friday. Fundus examination and tonometry were determined by a single skilled expert. Glaucomatous optic nerve alteration, nerve fiber layer alteration, a vertical cup-disc ratio ≥0.6, caving of the optical disc, acquired optical disc cupping, optic disc hemorrhage, and other retinal diseases were excluded from fundus examination.

The IOP of the right eye was determined, as the left and right eyes showed a high correlation (correlation coefficient r=0.85, P<0.001). When measured IOP was >21 mm Hg and the visual field examination results and optic disc were diagnosed as normal, the subject was defined as having “ocular hypertension”. Glaucomatous optic nerve head damage was defined as cup-to-disc ratio asymmetry of >0.2 between fellow eyes or a rim notch with a rim width ≤0.1 disc diameters. SITA-standard program was used to evaluate central 30-2 perimetry (Humphrey field analyzer; Carl Zeiss Meditec, Dublin, CA, USA). A glaucomatous visual field defect was defined as the consistent presence of a cluster of ≥3 contiguous non-edge points on the pattern deviation plot with a probability of occurring in <5% of the normal population (P<0.05), with one of these points having a probability of occurring in <1% of the normal population (P<0.01), or a glaucoma hemifield test result outside the normal limits. Propensity score matching with age and sex was used to select controls to compare the ocular hypertension group with the normal IOP group[11]. An independent sample t-test was used to compare the 2 IOP groups, univariate and multiple regression tests were used to compare the correlation between obesity-related health factors and IOP, and multiple logistic regression analysis after adjusting for age and sex was used to calculate odds ratio between ocular hypertension and morbidly obesity with normal IOP as the reference group. All statistical analyses were conducted using measurements from the right eye, with PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). A P value <0.05 was considered statistically significant.

RESULTS

Subjects in the ocular hypertension group included 1515 of 40850 people (3.7%) with an IOP of >21 mm Hg as measured by a non-contact tonometer. For comparison, 1515 people with normal IOP were randomly chosen using propensity score matching with age and sex according to ocular hypertension. Of 3030 people, 2067 (68.22%) were men and 963 (31.8%) were women. The mean age was 47.2±10.4y: 687 (22.7%) were aged <40y, 1144 (37.6%) were aged 40-49y, 820 (27.1%) were aged 50-59y, 379 (12.6%) were aged ≥60y (Figure 2).

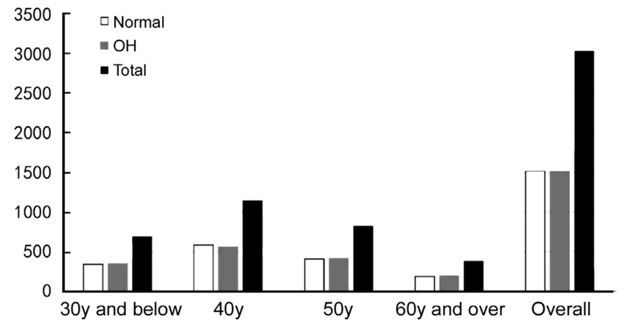

Figure 2 The composition and age distribution of participants with normal IOP and ocular hypertension OH: Ocular hypertension.

Table 1 Comparison of variable parameters between the normal IOP group and ocular hypertension group

Patient characteristics	Normal IOP group	Ocular hypertension group	P
No. of patients	1515	1515	
Sex (male:female)	1049:466	1018:497	0.227
Mean age (y)	47.2±10.4	47.1±10.5	0.782
IOP (mm Hg)	15.3±2.3	23.3±1.6	<0.001[a]
SBP (mm Hg)	130.9±19.3	131.4±19.3	0.525
DBP (mm Hg)	81.1±22.6	81.1±11.8	0.966
Height (cm)	166.53±8.00	165.15±8.35	<0.001[a]
Body weight (kg)	67.66±10.62	67.40±11.21	0.501
Standard body weight (kg)	59.87±7.20	58.64±7.52	<0.001[a]
Waist circumference (cm)	84.13±8.82	84.38±8.80	0.422
Obesity index	113.35±14.10	115.24±14.44	<0.001[a]
BMI (kg/m^2)	24.34±2.95	24.62±3.03	0.009[a]
ASBI	0.777±0.042	0.777±0.040	0.819
WHtR	0.506±0.053	0.511±0.052	0.002[a]

IOP: Intraocular pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; ABSI: A body shape index; WHtR: Waist-to-height ratio. [a]Statistical significant.

The mean IOP was 19.3±4.6 mm Hg (19.3±4.6 mm Hg in men and 19.2±4.6 mm Hg in women). There was no significant difference in IOP between the two sexes (P=0.613).

In normal IOP group, the mean age was 47.2±10.4y and the mean IOP was 15.3±2.3 mm Hg, whereas the mean age was 47.1±10.5y and the mean IOP was 23.3±1.6 mm Hg in the ocular hypertension. There was a significant difference in mean IOP between the normal IOP and ocular hypertension groups (P<0.001). The height and the mean standard body weight, which is another obesity-related factor had the significant difference between normal IOP and ocular hypertension groups (P<0.001 in both). The obesity index (113.35±14.10 *vs* 115.24±14.44; P<0.001), BMI (24.34±2.95 kg/m^2 *vs* 24.62±3.03 kg/m^2; P=0.009) and WtHR (0.506±0.053 *vs* 0.511±0.052; P=0.002) were all significantly higher in the ocular hypertension than in normal group. However, there was no significant difference in ABSI (0.777±0.042 *vs* 0.777±0.040; P=0.819) between the two groups (Table 1).

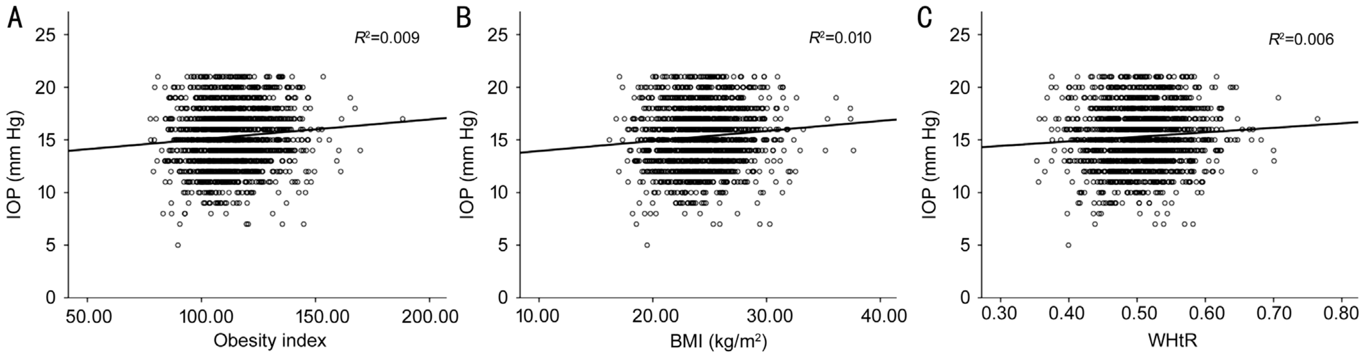

Figure 3 Univariate regression analysis between IOP and obesity index (A), BMI (B), and WHtR (C) in the normal IOP group Obesity index ($P<0.001$), BMI ($P<0.001$), and WHtR ($P=0.002$) were positively correlated with IOP.

Table 2 Comparison of obesity related factors between normal IOP group and ocular hypertension group

Age group	IOP group	*n*	Obesity index	BMI	ASBI	WHtR
Under 30y	Normal	338	110.94±15.80	24.03±3.50	0.760±0.038	0.486±0.054
	OH	349	113.80±15.57	24.58±3.50	0.761±0.038	0.496±0.054
	P		0.017[a]	0.039[a]	0.599	0.016[a]
40y	Normal	584	113.14±13.08	24.35±2.77	0.773±0.041	0.502±0.048
	OH	560	113.88±13.65	24.41±2.92	0.774±0.037	0.505±0.048
	P		0.349	0.709	0.537	0.249
50y	Normal	406	114.89±14.12	24.51±2.83	0.785±0.038	0.516±0.051
	OH	414	116.73±14.08	24.78±2.84	0.784±0.039	0.521±0.052
	P		0.062	0.176	0.591	0.170
Over 60y	Normal	187	115.00±13.30	24.48±2.60	0.806±0.044	0.530±0.052
	OH	192	118.66±14.56	24.98±2.83	0.799±0.038	0.537±0.051
	P		0.011[a]	0.075	0.090	0.182
Total	Normal	1515	113.35±14.10	24.34±2.95	0.777±0.042	0.506±0.053
	OH	1515	115.24±14.44	24.62±3.03	0.777±0.040	0.511±0.052
	P		<0.001[a]	0.009[a]	0.819	0.002[a]

IOP: Intraocular pressure; OH: Ocular hypertension; BMI: Body mass index; ABSI: A body shape index; WHtR: Waist-to-height ratio. [a]Statistical significant.

There was a significant difference between the two groups among people aged 39y and below, and total age ranges, in obesity index ($P=0.017$, $P<0.001$), BMI ($P=0.039$, $P=0.009$), and WtHR ($P=0.016$, $P=0.002$). Only the obesity index ($P=0.011$) was significantly different in people aged ≥60y (Table 2).

In the normal IOP group, univariate regression analysis showed that body weight ($P=0.001$), SBP and DBP ($P<0.001$, $P=0.002$), waist circumference ($P=0.001$), obesity index ($P<0.001$), BMI ($P<0.001$), and WHtR ($P=0.002$) were positively correlated with IOP (Table 3, Figure 3). Obesity index ($P=0.027$), and BMI ($P=0.016$) were positively correlated with IOP in the ocular hypertension group (Table 3, Figure 4).

A multiple regression analysis was conducted to determine the factors that affected IOP after adjustment of other confounding variables, and this study included obesity-related health factors and anthropometric data that had a significant correlation.

When other variables were adjusted, SBP ($\beta=0.022$, $P<0.001$) and body weight ($\beta=0.016$, $P=0.02$) are directly associated with IOP in normal IOP group. The gender (male) was indirectly associated with IOP ($\beta=-0.231$, $P=0.008$) and obesity index was directly associated with IOP ($\beta=0.007$, $P=0.017$) in ocular hypertension group (Table 4).

A multiple logistic regression analysis after adjusting for age and sex was conducted to calculate odds ratio between ocular hypertension group and morbid obesity-related health factors with normal IOP group set as the reference group. Morbid obesity and related health parameters were defined based on the results of the previous studies[12-15].

In the multiple logistic regression analysis, hypertension was defined as SBP≥140 mm Hg or DBP≥90 mm Hg; High waist circumference was defined as waist circumference ≥90 cm in male, ≥85 cm in female; High obesity index was defined as obesity index ≥120; High BMI was defined as BMI ≥25 kg/m^2; High ABSI was defined as ABSI≥0.808; High WtHR was defined as WtHR≥0.63 in male, ≥0.58 in female[12-15].

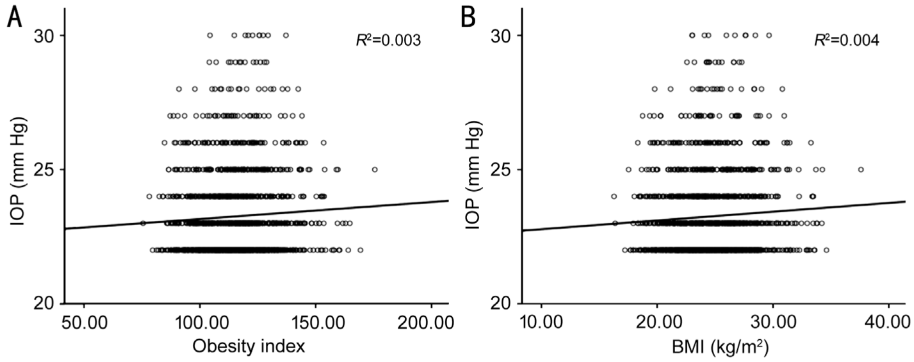

Figure 4 Univariate regression analysis between IOP and obesity index (A), and BMI (B) in ocular hypertension group Obesity index (P=0.027), and BMI (P=0.016) were positively correlated with IOP in the ocular hypertension group.

Table 3 The results of univariate regression analysis between IOP and variables including age, sex, and systemic factors

Variables	Normal IOP group		Ocular hypertension group	
	β±SE	P	β±SE	P
Sex (male)	-0.327±0.160	0.041[a]	-0.231±0.087	0.008[a]
Age (y)	-0.003±0.007	0.638	-0.006±0.004	0.123
Height (cm)	0.006±0.009	0.548	0.002±0.005	0.671
SBP (mm Hg)	0.022±0.004	<0.001[a]	0.004±0.002	0.095
DBP (mm Hg)	0.010±0.003	0.002[a]	0.003±0.003	0.435
Body weight (kg)	0.024±0.007	0.001[a]	0.007±0.004	0.05
Standard body weight (kg)	0.006±0.010	0.548	0.002±0.005	0.671
Waist circumference (cm)	0.027±0.008	0.001[a]	0.009±0.005	0.061
Obesity index	0.019±0.005	<0.001[a]	0.006±0.003	0.027[a]
BMI (kg/m^2)	0.095±0.025	<0.001[a]	0.033±0.014	0.016[a]
ASBI	0.545±1.746	0.755	-0.069±1.036	0.947
WHtR	4.290±1.403	0.002[a]	1.328±0.785	0.091

IOP: Intraocular pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; ABSI: A body shape index; SE: Standard error; WHtR: Waist-to-height ratio. [a]Statistical significant.

Table 4 The results of multiple regression analysis between IOP and systemic factors in normal IOP group and ocular hypertension group

Variables	Normal IOP group			Ocular hypertension group		
	β±SE	Partial R^2	P	β±SE	Partial R^2	P
Sex (male)				-0.231±0.087	0.008	0.008[a]
SBP (mm Hg)	0.022±0.004	0.026	<0.001[a]			
BW (kg)	0.016±0.007	0.026	0.02[a]			
Obesity index				0.007±0.003	0.008	0.017[a]

IOP: Intraocular pressure; SBP: Systolic blood pressure; BW: Body weight; SE: Standard errors. [a]Statistical significant.

We found that high obesity index was a significant risk factor for ocular hypertension (odds ratio, 1.306; 95%CI, 1.121-1.522; Table 5).

Table 5 Multiple logistic regression analysis for the association between ocular hypertension group and morbidly obesity-related health factors

Variables	ORs	95%CI	P
Hypertension	1.018	0.871-1.190	0.823
High waist circumference	0.917	0.736-1.141	0.437
High obesity index	1.306	1.121-1.522	0.001[a]
High BMI	1.116	0.874-1.425	0.378
High ABSI	0.915	0.754-1.109	0.365
High WtHR	1.195	0.799-1.787	0.386

ORs: Odds ratio. [a]Statistical significant.

DISCUSSION

IOP is an important indicator in the diagnosis and treatment of glaucoma. When IOP is greater than 21 mm Hg without signs of a glaucomatous visual field or damage to the optic disc, close observation is required because there is a possibility of primary open angle glaucoma[3,16].

Many factors affect IOP, including age, sex, family history, race, blood pressure, and systemic diseases such as diabetes.

Obesity increases adipose tissue in eye sockets, increases episcleral venous pressure and corticosteroid secretion, and decreases aqueous outflow due to excessive blood viscosity, which can result in high IOP[17-19]. Obesity is also related to diseases that affect ocular hypertension, hypertension, diabetes, and dyslipidemia[19]. Moreover, many epidemiologic studies have detected positive correlation between obesity-related parameters and high IOP[10,17,20].

In this study, a non-contact tonometer was used instead of Goldmann applanation tonometry, which is primarily used when determining IOP. Although there was some bias between the non-contact tonometer and the applanation tonometer, the two are known to show relatively similar IOP results[21-22]. This study revealed a significant difference in mean IOP between the two groups: 15.3±2.3 mm Hg in normal IOP group, and 23.3±1.6 mm Hg in ocular hypertension group, which is similar to IOP ranges reported in previous studies[8,10,20,23]. According to this study, 3.7% of all study subjects had ocular hypertension greater than 21 mm Hg, and previous reports showed 4.5%-10% in white patients, 3.7% in Pakistani patients, 2.1%-4.22% in Korean patients, and 2.0% in Japanese patients, and all patients showed similar distributions[10,12,23].

The Western population showed positive correlation between age and IOP[24-25], while the Asian populations in Japan and Korea showed negative correlation[10,18,26]. By this study, both normal IOP and ocular hypertension group showed negative correlation between age and IOP, but there was no statistical significance.

When comparing IOP and sex, women had higher IOP than men in a normal Japanese population[18], while in India, men had higher IOP than women[27]. We found that being male was significantly associated with low IOP in ocular hypertension after adjustment of SBP, body weight, and obesity index. It seemed that IOP might influence according to the ratio of sex, as more study subjects were men. Additional epidemiological surveys with equal sex ratios are required. Overall, many epidemiologic studies showed variable results, which seems to be due to racial or sex differences, environmental differences, and genetic factors[19,26,28].

The obesity index, BMI, and the WtHR were positively correlated with IOP after adjusting for age, sex, and blood pressure in ocular hypertension and normal IOP groups[8,29]. Among obesity-related factors, most epidemiological reports have studied obesity index or BMI. However, there was some confusion regarding the direct effectiveness of the obesity index or BMI, regarding whether it reflected the actual muscle/fat ratio and could be used to predict the danger of abdominal obesity[29-31].

We found that factors which were significantly associated with IOP included SBP and body weight in the group with normal IOP, and sex (male) and obesity index in the group with ocular hypertension.

This study also shows that there are significant correlations between obesity index, BMI, WtHR, and IOP. According to a comparative study, the obesity index, BMI, and WtHR correlated with IOP in normal IOP group, and the obesity index and BMI correlated with IOP in ocular hypertension group. Within the range of normal IOP, obesity-related factors and IOP showed a similar relationship[8-10,18].

Regarding predictable factors of IOP, SBP and body weight are the effective influencing factor in normal IOP group, whereas the obesity index seemed to be the predictable factor in ocular hypertension group[8,10]. According to this study, the obesity index and BMI are both correlated with high IOP, even in confirmed cases of ocular hypertension. We found that the obesity index is a significant risk factor for ocular hypertension. In our study, individuals with high obesity index are significantly more likely to have ocular hypertension compared with normal IOP. An obesity index greater than 120% is defined as high obesity index and an indicator of morbid obesity[12]. This is consistent with a large study of 93 703 Japanese[26], indicating that higher obesity index was associated with higher IOP. By the cross-sectional analysis of this study, it has limits in determining causal relationship between obesity-related health parameters and IOP. As correlations between central corneal thickness or waist-hip ratio (which is currently linked to cardiovascular disease) have not been evaluated, additional wide epidemiological surveys are required.

With changes in Western dietary habits, the incidence of obesity has steadily increased. Thus, epidemiological studies regarding physiologic mechanisms between obesity and IOP are very important. According to this study of ocular hypertension, the obesity index plays an important role in the pathogenesis of ocular hypertension. Therefore, control of obesity seems to be a key factor in control of ocular hypertension, which if unchecked could lead to glaucoma.

ACKNOWLEDGEMENTS

Conflicts of Interest: Ahn MW, None; **Lee JW,** None; **Shin JH,** None; **Lee JS,** None.

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