Heritabilities of Intraocular Pressure in the Population of Korea
The Korean National Health and Nutrition Examination Survey 2008-2009

Na Rae Kim, MD; Hyun Ju Park, MS; Young Ju Suh, PhD; Hee Seung Chin, MD, PhD; Chan Yun Kim, MD, PhD

IMPORTANCE Intraocular pressure (IOP) is the principal modifiable risk factor for the progression of primary open-angle glaucoma. Studies that have measured the IOP directly in large numbers of matched parent-offspring pairs are limited in Asian populations.

OBJECTIVE To compare IOPs in parents and their offspring in Korea.

DESIGN, SETTING, AND PARTICIPANTS Family-based cohort study examining data from the Korean National Health and Nutrition Examination Survey conducted between 2008 and 2009. Data were obtained from 9700 participants from Korea.

MAIN OUTCOMES AND MEASURES Familial correlations for IOP were calculated in different types of relative pairs. Variance component methods were used to obtain heritability estimates. The individuals were stratified into 2 groups (those with and those without an IOP of \( \geq 19 \) mm Hg, ie, high IOP group and nonhigh IOP group) based on the mean plus 2 SD IOP value of the entire study population. We evaluated the impact of parents' high IOP on offspring's high IOP. The relationship between parental systemic disease and high IOP in their offspring was also investigated.

RESULTS The mean (SD) IOPs in the right and left eyes were 13.90 (2.74) and 13.89 (2.74) mm Hg, respectively. Correlation coefficient estimates between parent-offspring pairs, sibling pairs, and spouse pairs for IOP were significant as 0.19, 0.31, and 0.29 (\( P < .001, P = .001, \) and \( P < .001, \) respectively). The total variance of the phenotype under study was explained by 2 sources of variation, additive genetic (36% [95% CI, 32%-40%]) and unique environment (64% [95% CI, 60%-68%]). The risks of high IOP conferred by parents' high IOP were found to be significant for participants whose parents had high IOP (odds ratio, 9.76 [95% CI, 2.16-44.12]). In this study, high IOP was not associated with parental diabetes mellitus, hypertension, obesity, or metabolic syndrome.

CONCLUSIONS AND RELEVANCE Intraocular pressure showed a significant heritable tendency from parents to their offspring with a heritability estimate of 0.36 in Asian populations. The risk of high IOP was significantly increased in participants whose parents had high IOP. This has potential implications for the screening of family members of patients with ocular hypertension and glaucoma.
Intraocular pressure (IOP) is the principal modifiable risk factor for the progression of primary open-angle glaucoma. Because open-angle glaucoma is often asymptomatic until the disease is relatively advanced, identifying youths with risk factors associated with the progression of glaucoma would be helpful.

Parents affect their offspring both genetically and environmentally. In twin studies, IOP showed a stronger correlation with monozygotic twins than dizygotic twins. The reported heritability of IOP, which is defined as the proportion of variance attributed to genetic factors based on family data, ranges from 30% to 50%, and the estimates based on twin pairs are greater than 60%.

The prevalence of primary glaucoma and the distribution of IOPs in East Asian populations appear to be somewhat different from those in white populations. Although previous studies reported a modest positive correlation of the IOP between both parent-offspring and siblings through a population-based cohort, studies that have measured the IOP directly in large numbers of matched parent-offspring pairs are limited. The current knowledge on how the IOP correlates between parents and their offspring generally does not consider the confounding variables affecting the level of IOP, such as hemodynamic and metabolic abnormalities.

Our study examined the association of IOP between offspring and their parents in an Asian population, adjusting for important confounding variables. The associations of IOP with participant and parental diabetes, hypertension, obesity, and metabolic syndrome were also examined.

Methods

Participants
A description of the participants is reported elsewhere. The Korean National Health and Nutrition Examination Survey (KNHANES) is an ongoing population-based, cross-sectional epidemiological survey conducted by the Korean Ministry of Health and Welfare. This ophthalmologic survey was conducted over a 5-year period, which began in 2008 and finished in 2013. The data in our study were obtained from the KNHANES between July 2008 and December 2009. Our study was approved by the institutional review board of the Korea Centers for Disease Control and Prevention (approval numbers 2008-01EXP-08-P and 2009-01CON-03-2C) and all study participants provided written informed consent.

Measurements of IOP and Other Traits

The participants underwent full ocular examinations, including measurement of visual acuity, refraction, and IOP, as well as slitlamp examinations and fundus examinations with photographs. Bilateral IOP was measured once in the morning between 8:00 AM and noon by Goldmann applanation tonometry (Haag-Streit) by an individual masked to the relationship between parents and offspring. The IOP measurements were taken with the patient in a seated position, following administration of a topical anesthetic drop with fluorescein in both eyes. Participants who used antiglaucoma medication and/or who underwent laser trabeculoplasty or glaucoma surgery were excluded because these medications or procedures can affect the IOP. Pseudophakic or aphakic patients were also excluded. Participants with light perception or no light perception vision were also excluded (Figure 1).

As part of the examination, the height, weight, waist circumference, systolic blood pressure, diastolic blood pressure, and fasting serum glucose, triglyceride, total cholesterol, high-density lipoprotein cholesterol, and insulin levels were measured using conventional methods. Obesity was defined as a body mass index, calculated as weight in kilograms divided by height in meters squared, greater than 25. Diabetes mellitus was defined as a fasting glucose level of at least 126 mg/dL (to convert to millimoles per liter, multiply by 0.0555) or the current use of antidiabetic medications. The participants were defined as hypertensive if their systolic blood pressure was 140 mm Hg or higher, if their diastolic blood pressure was 90 mm Hg or higher, or if they were already taking antihypertensive medication. Metabolic syndrome was defined based on a recently harmonized definition as the presence of 3 or more of the following components: (1) central obesity (waist circumference, >90 cm in men and >85 cm in women), (2) a fasting triglyceride level of 150 mg/dL or higher (to convert to millimoles per liter, multiply by 0.0555) or specific treatment, (3) a fasting glucose level of 100 mg/dL or higher or specific treatment, (4) systolic blood pressure of 130 mm Hg

Figure 1. Enrollment of Study Participants

20277 Participants from KNHANES 2008-2009
15071 Participants older than 19 years of age
5371 Excluded
3739 IOP data unavailable
73 Participants who had any glaucoma treatment (antiglaucoma medication, laser trabeculoplasty, or glaucoma surgery)
579 Pseudophakic patients
8 Aphakic patients
21 Participants who had visual acuity of light perception
4772 Any data missing in covariates (age, sex, refractive error, BMI, SBP, glucose, and total cholesterol)
9700 Included in analysis
2077 Included in subanalysis (both maternal and paternal data available)
(624 fathers, 624 mothers, 431 sons, and 398 daughters)

Many participants were excluded based on 2 or more of the exclusion criteria provided; therefore, the numbers of participants excluded owing to various criteria do not add up to 5371. BMI indicates body mass index; IOP, intraocular pressure; KNHANES, Korean National Health and Nutrition Examination Survey; and SBP, systolic blood pressure.
or higher, diastolic blood pressure of 85 mm Hg or higher, or specific treatment, and (5) a high-density lipoprotein cholesterol of less than 40 mg/dL in men and less than 50 mg/dL in women or specific treatment.

Statistical Analyses
For quantitative analyses, the eye with the higher IOP measurement was selected if the contralateral eye had a lower IOP.22 If the IOP in one eye was equal to that in the other eye, a randomly selected eye was used for analyses. The higher IOP measurement from either eye was used in these analyses because higher IOP is a practical parameter associated with higher risk of damage to the optic nerve.22 Intraocular pressure was analyzed as a continuous variable for estimating the familial correlations and heritability.

Familial correlation coefficients were estimated using the FCOR and ASSOC software programs (S.A.G.E.—Statistical Analysis for Genetic Epidemiology, version 6.2 [2012]; http://darwin.cwru.edu/sage). Correlation coefficients were calculated in the following pairs: parent-offspring, siblings, spouses, and grandparent-offspring. Comparison of familial correlation between different relative pairs allowed for the determination of the relative contributions of genetic and environmental effects.

Heritability was calculated as the proportion of the total phenotypic variance explained by additive genetic effects using variance-component analysis in Sequential Oligogenic Linkage Analysis Routines (SOLAR version 4.3.1, assessed September 2012). The residual variance (σ²) was partitioned into 3 components: additive genetic factors (A), common environmental factors (C), and unique environmental factors (E). Heritability (h²) was defined as the ratio of the residual variance of the trait resulting from the additive genetic factor (A) compared with the total residual phenotypic variance (σ²). The full ACE model was initially fit to the data and then compared with 3 submodels: one submodel included additive genetic and unique environmental factors (AE), another submodel included common and unique environmental effects (CE), and the final submodel included unique environmental factors (E).

The significance of variance was assessed by removing each component in the submodels and testing the deterioration of the model fit after each component was dropped from the full ACE model. The fit of each submodel was evaluated by use of the likelihood ratio test.

The individuals were stratified into 2 groups (those with and those without an IOP of ≥19 mm Hg) based on the mean plus 2 SD IOP value of the entire study population. The association between parents’ high IOP and offspring’s high IOP was assessed using the χ² test and logistic regression analyses. The mean IOP according to the status of the parents’ IOP was compared using analysis of variance. The relationship between parental systemic disease and high IOP in their offspring was also investigated. The analyses were conducted after adjusting for the potential confounding effects of offspring age, sex, refractive error, body mass index, systolic blood pressure, and fasting serum glucose and total cholesterol levels. Statistical analyses were performed using SPSS version 19.0 software (SPSS Inc).

Results
From July 2008 to December 2009, a total of 15,071 participants older than 19 years of age were supposed to have undergone a full ophthalmic examination. At the end of the selection procedures (Figure 1), 9,700 participants were included in our study. Table 1 lists the baseline characteristics of the study population. In this study population (from 19 to 91 years of age), the mean (SD) IOPs in the right and left eye were 13.90 (2.74) and 13.89 (2.74), respectively.

Table 2 lists estimated correlation coefficients for IOPs for each type of family relationship. The correlation coefficient for IOPs between siblings was estimated to be 0.31 (95% CI, 0.24–0.39), that between parents and offspring was 0.19 (95% CI, 0.16–0.22), and that between spouses was 0.29 (95% CI, 0.24–0.34). Correlations between the 2 types of first-degree relatives (sibling pairs and parent-offspring pairs) who share the same amount of genetic information (50%) were different, providing evidence for the existence of environmental effects. On the other hand, the difference was not significant (P = .11), which suggests that genetic effects do contribute to IOP. The relatively low correlations, even for sibling pairs, suggested that a large proportion of the residual variance is due to unshared effects. Familial correlations for spouse pairs (who shared no genetic information) were positive. Similar correlation coefficients for familial pairs and spousal pairs were observed.

### Table 1. Characteristics of the 9,700 Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>48.5 (16.4)</td>
</tr>
<tr>
<td>Ocular parameters</td>
<td></td>
</tr>
<tr>
<td>Right eye IOP, mm Hg</td>
<td>13.9 (2.7)</td>
</tr>
<tr>
<td>Left eye IOP, mm Hg</td>
<td>13.9 (2.7)</td>
</tr>
<tr>
<td>Higher IOP between both eyes, mm Hg</td>
<td>14.4 (2.7)</td>
</tr>
<tr>
<td>Refractive error,* D</td>
<td>−0.9 (2.2)</td>
</tr>
<tr>
<td>Anthropometrics</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>23.6 (3.3)</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>81.2 (9.9)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>116.8 (17.5)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>75.0 (10.7)</td>
</tr>
<tr>
<td>Metabolites, mg/dL</td>
<td></td>
</tr>
<tr>
<td>Fasting serum glucose</td>
<td>97.9 (24.1)</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>133.6 (105.6)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>187.0 (35.7)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>47.3 (10.8)</td>
</tr>
<tr>
<td>Insulin, µIU/mL</td>
<td>9.8 (6.2)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); D, diopters; DBP, diastolic blood pressure; HDL, high-density lipoprotein; IOP, intraocular pressure; SBP, systolic blood pressure.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; to convert triglyceride to millimoles per liter, multiply by 0.0113; to convert total and HDL cholesterol to millimoles per liter, multiply by 0.0259; and to convert insulin to picomoles per liter, multiply by 6.945.

* Refractive status of the eye with a higher IOP.
(P = .07 for parent-offspring pairs vs spouse pairs; P = .84 for sibling pairs vs spouse pairs). Assortative mating is one possible explanation for the positive correlations observed in spouses. Spouses might be similar in age, body weight, and other variables. Environmental factors that are shared by spouses offer an alternative explanation.

To estimate heritability, we first used the model with the 3 components (ie, model ACE) and then tested that against a model AE without the common environmental component (C). The mean (SE) heritability ($h^2$) estimate, adjusted for age, sex, refractive error, body mass index, systolic blood pressure, and fasting serum glucose and total cholesterol levels from the ACE model, was 0.345 (0.046). Shared environmental factors accounted for 8.1% of the total variation in IOP. When the common environment component (C) was excluded from the ACE model, the mean (SE) heritability increased slightly to 0.361 (0.043) without a significant decrease in fit ($\Delta \chi^2 = 1.673, P = .10$). Therefore, the total variance in IOPs can be explained by 2 sources of variation, the additive genetic ($A; 36\% [95\% CI, 32%-40\%]$) and unique environment ($E; 64\% [95\% CI, 60%-68\%]$) components. The CE model, containing both common and unique environment sources of variation, the additive genetic ($A; 36\% [95\% CI, 32%-40\%]$), and unique environmental components, was significantly different from the ACE model ($P < .001$). Dropping A from the ACE model caused a change in fit by $\Delta \chi^2 = 51.133, P < .001$.

Therefore, the status of a parent’s IOP significantly increased as the number of parents with a high IOP increased. The prevalence of a high IOP in the offspring without a parent with a high IOP, in the offspring with 1 parent with a high IOP, and in the offspring with both parents with a high IOP was 6.5%, 17.4%, and 76.1%, respectively. The odds ratios for a high IOP were 1.69 (95% CI, 0.75-3.81) and 9.76 (95% CI, 2.16-44.13) in the offspring with 1 parent and in the offspring with both parents with a high IOP, respectively, compared with the offspring without a parent with a high IOP, after adjusting for the covariates. A dose-response relationship was found in these analyses (Table 4).

When the mean IOP was compared according to the status of a parent’s IOP, the mean IOP was lowest in the eyes of offspring with both parents with a high IOP and was highest in the eyes of offspring with both parents with a high IOP ($P < .001$). We then compared the mean IOP according to the status of a parent’s IOP between the subgroups with nonhigh IOP and the subgroups with high IOP. In the group with non-high IOP, the mean IOP was significantly different according to the status of a parent’s IOP ($P < .001$) and was highest in the

### Table 2. Familial Correlation of a Parent’s Intraocular Pressure With an Offspring’s Intraocular Pressure

<table>
<thead>
<tr>
<th>Correlation</th>
<th>Count</th>
<th>Estimated Correlation Coefficient (95% CI)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent-offspring</td>
<td>1520</td>
<td>0.19 (0.16-0.22)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mother-daughter</td>
<td>413</td>
<td>0.17 (0.12-0.22)</td>
<td>.001</td>
</tr>
<tr>
<td>Father-daughter</td>
<td>292</td>
<td>0.12 (0.06-0.18)</td>
<td>.04</td>
</tr>
<tr>
<td>Mother-son</td>
<td>522</td>
<td>0.24 (0.19-0.28)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Father-son</td>
<td>293</td>
<td>0.20 (0.14-0.26)</td>
<td>.001</td>
</tr>
<tr>
<td>Siblings</td>
<td>164</td>
<td>0.31 (0.24-0.39)</td>
<td>.001</td>
</tr>
<tr>
<td>Sister-sister</td>
<td>52</td>
<td>0.26 (0.12-0.40)</td>
<td>.08</td>
</tr>
<tr>
<td>Sister-brother</td>
<td>75</td>
<td>0.25 (0.13-0.36)</td>
<td>.04</td>
</tr>
<tr>
<td>Brother-brother</td>
<td>37</td>
<td>0.49 (0.36-0.62)</td>
<td>.001</td>
</tr>
<tr>
<td>Spouses</td>
<td>333</td>
<td>0.29 (0.24-0.34)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Grandparents-offspring</td>
<td>29</td>
<td>0.42 (0.25-0.59)</td>
<td>.03</td>
</tr>
</tbody>
</table>

### Table 3. Heritability Estimates for Intraocular Pressure Based on Parent-Offspring Regression Analysis

<table>
<thead>
<tr>
<th>Model</th>
<th>$c^2$ [95% CI]</th>
<th>$c^2$ [95% CI]</th>
<th>$e^2$ [95% CI]</th>
<th>$\Delta \chi^2$</th>
<th>$\Delta df$</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>0.345 (0.046)</td>
<td>0.081 (0.062)</td>
<td>0.574 (0.064)</td>
<td>9424.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AE</td>
<td>0.361 (0.043)</td>
<td>0.091 (0.062)</td>
<td>0.569 (0.064)</td>
<td>9425.9</td>
<td>1</td>
<td>.10</td>
</tr>
<tr>
<td>CE</td>
<td>0.264 (0.057)</td>
<td>0.736 (0.057)</td>
<td>0.976 (0.064)</td>
<td>9475.3</td>
<td>51.133</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>E</td>
<td>1</td>
<td></td>
<td></td>
<td>9494.1</td>
<td>69.870</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: A, additive genetic influences; $c^2$, proportion of variance explained by additive genetic influences; C, shared environmental influences; $c^2$, proportion of variance explained by shared environmental influences; E, nonshared environmental influences; $e^2$, proportion of variance explained by nonshared environmental influences.

* Values adjusted for covariates (age, sex, refractive error, body mass index, systolic blood pressure, and fasting serum glucose and total cholesterol levels).

$\Delta \chi^2$ obtained from a likelihood ratio test of the AE, CE, or E model compared with the ACE model.
eyes of offspring with both parents with a high IOP. In the group with high IOP, the mean IOP was statistically similar regardless of their parents’ IOP (P = .23) (Table 5; Figure 2).

Table 6 shows the relationship between the offspring with high IOP and parental diabetes mellitus, hypertension, obesity, and metabolic syndrome. After adjusting for covariates, we found that none of the parental systemic diseases were significantly associated with high IOP in offspring (P > .05).

Discussion

Our study investigated the familial correlations and heritabilities of IOP. The trends from familial correlations suggested that the variance in IOPs is affected by both genetic and environmental factors. The results of the full variance component models confirmed the predominantly genetically determined variance with the significant heritabilities for IOP. The prevalence of high IOP in offspring increased with the increasing number of parents with high IOP. The odds ratio for a high IOP (≥19 mm Hg) was 9.76 in offspring with both parents with high IOP. This shows the relationship between the offspring with high IOP and parental diabetes mellitus, hypertension, obesity, and metabolic syndrome.

Studied that conducted visual field testing on all white participants and did not require an elevated IOP as a criterion for diagnosis suggest that the prevalence of glaucoma is between 1.5% and 2.0% for those 40 years or older.32 From the KHNES 2008-2009, the mean (SD) prevalence of glaucoma was 1.4% (0.1%) for participants older than 19 years of age and 2.1% (0.2%) for participants 40 years of age.19 The prevalence of glaucoma in this study was similar to that in population-based studies.29,30,33 These participants were not excluded from the present analysis. Individuals were excluded if they had used antiglaucoma medication at the time of the survey and/or had undergone laser trabeculectomy or glaucoma surgery.

Currently identified glaucoma-susceptibility genes contribute to pathogenesis in only a minority of cases.34-36 Given the relative rarity of glaucoma in the population, researchers have focused on the intermediate traits of glaucoma, such as IOP.37 Genetic influences on the IOP are suggested by previous reports on the linkage and genome-wide studies of IOP.23,38-44 This suggests that IOP may contribute to the heritable component of complex ocular disease and might be particularly important in primary open-angle glaucoma, in which the IOP is believed to be one of the most important independent risk factors.

The tendency of high IOP to aggregate within families could be explained by a culturally transmitted, shared family environment or an inherited genetic susceptibility to the shared environment. In human studies, the most important sources of confounding with additive genetic factors are shared environmental factors among relatives. The clustering of high IOP within a family may be attributed to a culture of shared risk factors, such as eating habits, residential environment, smok-
ing, and alcohol consumption, or shared susceptibility genes for high IOP in the family. In a previous study, higher body mass, seasonality, current alcohol use, and current smoking were factors positively related to IOP. In another study, from univariate analysis, elevated IOP was significantly related to the patient’s blood pressure treatment, level of education, and use of a hat and/or umbrella. Studies examining the effects of activities on IOP reported that exercise caused a clinically significant decrease in IOP.47,48 Further epidemiological studies may be necessary to determine other environmental contributors to IOP.

Familial correlations for spouse pairs were positive for IOP. The positive correlations observed for spouses could be due to shared environmental effects since marriage. Another possibility is that IOP was likely to be correlated at the time of marriage. In humans, assortative mating occurs along many dimensions, including, among others, age, physical traits, socioeconomic status, and intelligence.49 To further quantify the genetic component in families, heritability estimates and common environmental components of IOP were calculated. No significant effects of shared environmental factors were detected in the variance component model, as shown in Table 3.

In our study, the heritability estimates (ie, the proportion of the residual variance resulting from genetic components compared with the total residual phenotypic variance in the model AE) was approximately 36%. Previous family studies of IOP in white populations have suggested that genetic factors can explain approximately one-third of the variability in IOP.4-6 Twin cohort studies in Chinese, Finnish, and British (predominately white) populations have documented more than 60% heritability of IOP. At least part of this difference can be explained by differences in populations and study designs. Twin studies tend to show a higher heritability, in part due to the shared common environment that twins have.37 Ethnic differences can be another explanation for this discrepancy. Further investigation is needed of the genetic epidemiologic background of IOP using a large and more ethnically diverse population.

In subgroup analysis, the offspring with nonhigh IOP showed a significantly different mean IOP according to the status of a parent’s IOP (P < .001), whereas the offspring with high IOP showed a statistically similar mean IOP regardless of their parents’ IOP (P = .23). The observation might be due to the sample size difference between the 2 groups. The upper 97.5% limit (mean 2 SDs) of IOP was 19.4 mm Hg in our study. An IOP cutoff of 19 mm Hg was used to divide participants into subgroups. A disproportionate number of offspring might affect the results. Another possible explanation for the finding includes a “ceiling effect.” The IOPs were already high in the high IOP group, and there might be a little more room for a further increase depending on the status of a parent’s IOP.

Diabetes, hypertension, obesity, and metabolic syndrome have been associated with an elevated IOP, even though the current evidence to support these relationships is inconclusive. Several studies in Korea have shown that some components of metabolic syndrome are associated positively with IOP.7,59 In a recent study including the KNHANES data, IOP was significantly associated with metabolic syndrome in postmenopausal women but not in premenopausal women. In the present study, parental diabetes mellitus, hypertension, obesity, or metabolic syndrome did not have a significant relationship with the high IOP seen in their offspring. High heterogeneity of human diseases might explain

<table>
<thead>
<tr>
<th>Disease</th>
<th>Offspring, No. (%) (n = 829)</th>
<th>Unadjusted OR (95% CI)</th>
<th>P Value</th>
<th>Adjusted OR (95% CI)*</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal diabetes mellitus</td>
<td>68 (8.2)</td>
<td>1.070 (0.372-3.079)</td>
<td>.900</td>
<td>0.964 (0.326-2.853)</td>
<td>.95</td>
</tr>
<tr>
<td>Maternal hypertension</td>
<td>233 (28.1)</td>
<td>1.871 (1.019-3.435)</td>
<td>.04</td>
<td>1.735 (0.918-3.280)</td>
<td>.09</td>
</tr>
<tr>
<td>Maternal obesity</td>
<td>282 (34.0)</td>
<td>0.841 (0.441-1.603)</td>
<td>.60</td>
<td>0.859 (0.439-1.681)</td>
<td>.66</td>
</tr>
<tr>
<td>Maternal metabolic syndrome</td>
<td>215 (25.9)</td>
<td>1.008 (0.512-1.985)</td>
<td>.98</td>
<td>0.995 (0.491-2.015)</td>
<td>.99</td>
</tr>
<tr>
<td>Paternal diabetes mellitus</td>
<td>119 (14.4)</td>
<td>0.716 (0.277-1.849)</td>
<td>.49</td>
<td>0.641 (0.244-1.684)</td>
<td>.37</td>
</tr>
<tr>
<td>Paternal hypertension</td>
<td>334 (40.3)</td>
<td>1.261 (0.694-2.393)</td>
<td>.45</td>
<td>1.145 (0.612-2.145)</td>
<td>.67</td>
</tr>
<tr>
<td>Paternal obesity</td>
<td>321 (38.7)</td>
<td>1.121 (0.612-2.051)</td>
<td>.71</td>
<td>1.124 (0.597-2.116)</td>
<td>.72</td>
</tr>
<tr>
<td>Paternal metabolic syndrome</td>
<td>281 (33.9)</td>
<td>0.846 (0.444-1.612)</td>
<td>.61</td>
<td>0.787 (0.407-1.522)</td>
<td>.79</td>
</tr>
</tbody>
</table>

Abbreviation: OR, odds ratio.

* Adjusted for offspring’s age, sex, refraction error, body mass index, systolic blood pressure, and fasting serum glucose and total cholesterol levels.

ANOVA indicates analysis of variance; and IOP, intraocular pressure.
this result. The degree of resemblance among relatives varies according to the trait, depending on the combined effects of common environmental factors and inherited factors. The still unconfirmed influence of systemic disease on IOP might be another explanation for this result.

Our study had some limitations. First, our study was a cross-sectional study, so causation could not be inferred. Second, the data were based on single measurements of IOP, which could allow for measurement errors. Third, IOP was measured once in the morning, even though IOP is subject to cyclical fluctuations throughout the day. Fourth, the central corneal thickness itself has been re-measured once in the morning, even though IOP is subject to cyclical fluctuations throughout the day. Fourth, the central corneal thickness, which is a major determinant of IOP, was not measured. The central corneal thickness itself has been reported to be highly heritable. Fifth, the status of anterior chamber angle was not considered, even though angle-closure disease has a major impact on IOP. The KNHANES reported the prevalence of primary angle-closure glaucoma as 0.1%. Nevertheless, our study has particular strengths, among which is the use of data from a large, nationwide study population, in which each variable was measured directly between matched parent-offspring pairs.

Conclusions

Intraocular pressure appears to show significant parent-offspring heritability in a large family-based examination of an Asian population. The results indicated that additive genetic and unique environmental influences can best explain the variance in IOP, with approximately 36% (95% CI, 32%-40%) of the variance explained by genetic factors. The risk of a high IOP in offspring is associated with a high IOP in their parents. This knowledge has potential implications for the screening of family members of patients with ocular hypertension and glaucoma. Further studies are warranted to clarify Asian-specific characteristics of IOP.

REFERENCES

Heritabilities of IOP in the Population of Korea

Original Investigation Research


