# Distribution and Associations of Retinal Vascular Caliber with Ethnicity, Gender, and Birth Parameters in Young Children

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**Purpose.** To describe the distribution of retinal vascular calibers and their associations with ethnicity, gender, and birth parameters in children.

**Methods.** This was a school-based cross-sectional study of 768 children aged 7 to 9 years who participated in the Singapore Cohort Study of the Risk Factors for Myopia (SCORM). Participants had retinal photographs taken in 2001. Retinal vascular calibers were measured with computer-based program and summarized as average caliber of arterioles and venules in that eye. Associations of retinal vascular caliber with ethnicity, gender, and various birth factors were analyzed.

**Results.** In this population, the mean retinal arteriolar caliber was 156.4 μm (95% confidence interval [CI], 155.4–157.3) and venular caliber was 225.4 μm (95% CI, 224.1–226.8). The retinal arteriolar caliber was significantly narrower in Chinese (154.9 μm), compared with Malay (158.6 μm) and Indian (158.5 μm) children. Retinal venular caliber was also narrower in Chinese (223.3 μm) compared with Malay (230.8 μm) and Indian (229.0 μm) children. These differences were statistically significant, even after adjustments for age, gender, family income, parental education, body mass index, height, birth weight, axial length, and spherical equivalent ($P = 0.05$ for arteriolar caliber; $P = 0.002$ for venular caliber). In multivariate analysis, there were no significant gender differences in retinal vascular caliber. Birth factors, including birth weight, birth length, head circumference, and gestational age, were not significantly associated with changes in either retinal arteriolar or venular caliber.

**Conclusions.** The results show ethnic variation in retinal vascular caliber in Singaporean children. No association of birth parameters with retinal vascular caliber was found. Because retinal vascular caliber is related to various cardiovascular and ocular diseases, it is possible that ethnic variations in retinal vascular caliber should be taken into consideration in future studies. (*Invest Ophthalmol Vis Sci.* 2007;48:1018–1024) DOI:10.1167/iovs.06-0978

Emerging evidence suggests that in adult persons, changes in retinal vascular calibers (e.g., retinal arteriolar narrowing and venular dilatation) are correlated with a variety of vascular risk factors,[1–4] and may independently predict stroke[5,6] and other cardiovascular outcomes,[7–9] and ocular diseases such as glaucoma and diabetic retinopathy. Existing studies have largely focused on evaluating retinal vascular caliber changes in adults.

There are few studies on retinal vascular caliber and other structural characteristics in children. These studies indicate that variations in the vascular pattern may be associated with preterm birth[10–13] and several other conditions, such as fetal alcohol syndrome,[14] hypertension,[15] diabetes,[16] and endocrinopathy.[17] Some investigators have hypothesized that abnormal retinal vessels in preterm children reflect generalized vascular changes,[18] providing an explanation of why preterm children[11,19,20] and children with low birthweight[21,22] appear to have an increased risk of cardiovascular disease later in life.

Recently developed methods to measure retinal vascular caliber accurately from fundus photographs[23,24] have been successfully applied in several studies in adults.[7,9] However, one challenge in these studies is the difficulty in completely controlling for potential confounding related to systemic (e.g., hypertension, diabetes, medications, cigarette smoking) and ocular (e.g., glaucoma) factors. Children, who are generally free of influence from these processes, are ideal study populations for providing more accurate normative data on retinal vascular caliber. To the best of our knowledge, we are unaware of the application of these new imaging techniques to measure retinal vascular caliber in children.

In our present study, we described the distribution of retinal vascular calibers and their associations with ethnicity, gender, and birth parameters in a cohort of healthy school-aged children.

## Methods

### Study Population

The Singapore Cohort Study of Risk Factors for Myopia (SCORM) is a study of 1979 schoolchildren aged 7 to 9 years at baseline in Singapore. Details of the study population have been reported elsewhere.[25,26] In brief, 2913 children were initially recruited for the study with a participation rate of 67.9% (1979 participants). Children from grades 1 and 2 from an eastern school ($n = 660$) and children from grades 1, 2, and 3 from a northern school ($n = 1023$) were invited to participate in November 1999, and children from grades 1, 2, and 3 from a western school ($n = 1230$) were enrolled in May 2001. Children with serious medical conditions ($n = 94$), such as heart disorders, syndrome-

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associated myopia, or serious eye disorders, such as cataract, were excluded from the study.

From these three schools, 851 children, randomly and systematically sampled from the full cohort, were offered retinal photography in 2001. Retinal photographs were taken of at least one eye in 775 children. Compared with those without retinal photographs, children with gradable retinal photographs were more likely to be Chinese, myopic, and from a wealthier family background, and in addition, they were older, corresponding to the anthropometric differences (heavier, taller, greater body surface area, but similar BMI). All other characteristics were similar (data not shown). Children from non-Chinese/Malay/Indian or unknown ethnic-racial backgrounds ($n$ = 11), and those without anthropometric measurements ($n$ = 4) were excluded, leaving 760 participants for the analysis.

The Ethics Committee of the Singapore Eye Research Institute approved the study, and the conduct of the study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all parents after the nature of the study was explained.

## Retinal Photography

The children were examined on the school premises by a team of ophthalmologists, optometrists, and research assistants. After pupil dilatation with cyclopentolate 1%, digital retinal photographs centered on the optic disc were taken of both eyes using standardized settings (6.3 mega-pixel, resolution = 3072 × 2048; CR6-NM45, EOS-D60; Canon USA, Lake Success, NY).

The methods used to measure and summarize retinal vascular caliber from digitized photographs after standardized protocols have been described.[4,27] Briefly, a computer-based program was used to measure the caliber of all retinal vessels located 0.5 to 1 disc diameter from the optic disc margin in the digitized retinal photographs. Before measurement, an image conversion factor was derived from 50 randomly selected images, calculated as a standard vertical optic disc diameter (assumed to be 1800 μm[28–32]) divided by optic disc diameter in pixels. The conversation factor in this study was 7.67 μm per pixel. Individual retinal vascular caliber measurements from an eye were summarized as an average index according to formulas described elsewhere.[23,27,33] These indices, the central retinal arteriolar and venular equivalents (CRAE and CRVE), represented the average arteriolar and venular caliber of that eye.

One grader (KDH) masked to participant identity and characteristics performed all the retinal measurements. Retinal vascular caliber in the right eye was measured. Left eye measurements were performed when photographs of the right eye were ungradable. Remeasurement of 50 retinal images 2 weeks apart showed high reproducibility, with intraclass correlation coefficients of 0.853 for arteriolar caliber and 0.973 for venular caliber.

## Questionnaire and Birth Information

The parents completed several questionnaires, written in English or Chinese. Questions covered topics including demographic information, parental smoking status, and indicators of socioeconomic status, such as total family income per month, parental education level, and type of housing. Ethnicity was assessed by asking the parents to classify his or her ethnicity in the following groups: Chinese, Malay, or Indian. The ethnicity of the child was determined by using the father's reported ethnicity, according to the definition adopted by the Singapore Population Census 2000.[34] The child's birth history, including birth weight, birth length, head circumference, gestational age, and history of jaundice at birth, was obtained from a health booklet completed by medical personnel soon after birth.

## Collection of Other Information

Height and weight were measured on the school premises according to a standardized protocol. BMI was calculated as the weight divided by the square of the height (kg/m$^2$). Body surface area (BSA, m$^2$) was calculated according to the Mosteller formula: (height [cm] × weight [kg])/3600)$^{1/2}$.[35] Measurements of cycloplegic spherical equivalent (SE) refraction, logMAR visual acuity, and ocular biometric parameters have been described elsewhere.[25,26] SE refraction was defined as the spherical power plus half the negative cylinder power. Axial length, anterior chamber depth, lens thickness, and vitreous chamber depth measurements were obtained with a biometry ultrasound unit.

In 380 randomly selected children, blood pressure was measured in a seated position after 5 minutes of rest using an automated sphygmomanometer. The average of three separate measurements was used for analysis. Mean arterial blood pressure (MABP) was calculated as one third of the systolic blood pressure plus two thirds of the diastolic blood pressure.

## Statistical Analysis

We compared characteristics of children in different ethnic groups. Results were reported as means or proportions, with differences tested with ANOVA or $\chi^2$ tests, respectively. The mean retinal vascular calibers were compared within different ethnic and gender categories by using one way ANOVA. Analyses of covariance (ANCOVA) and linear regression models were used to determine the association of the birth parameters with retinal arteriolar and venular calibers. We initially used ANCOVA to estimate mean retinal caliber in association with presence versus absence of categorical variables (e.g., gestational age) or quartiles of continuous variables (e.g., birth weight). All initial models were adjusted for age, gender, and ethnicity.

We used multiple linear regressions to estimate the absolute changes in arteriolar and venular calibers for each standard deviation (SD) increase in birth weight, gestational age, birth weight, birth length, and head circumference at birth. We then constructed three models: Model 1 included adjustments for age, gender (not for gender analysis), ethnicity (not for ethnic analysis), family income and parental education; model 2 included additional adjustments for BMI, height, and birth weight; model 3 included additional adjustments for axial length and spherical equivalent; and model 4 had additional adjustments for mean arterial blood pressure (in the subgroup of 380 participants with blood pressure measurements).

All probabilities quoted are two sided, and all statistical analyses were undertaken with commercial software (SPSS ver. 12.0.1; SPSS Inc., Chicago, IL).

# Results

The mean age of the study population was 7.9 years, and 52.5% were boys. Selected characteristics and risk factors for each of the three ethnic groups among children who had retinal photographs ($n$ = 760) are shown in Table 1. There were significant differences in the frequency and distribution of several characteristics among the ethnic groups. For example, the Chinese children were generally younger and had shorter axial length than did the Malay and Indian children. In addition, the Chinese children were also more likely to be from wealthier and better-educated families. All other characteristics were similar.

In this population, the mean retinal arteriolar caliber was 156.4 μm (95% confidence interval [CI], 155.4–157.3) and venular caliber was 225.4 μm (95% CI, 224.1–226.8). Figure 1 illustrates a pattern of normal distribution for retinal arteriolar and venular calibers in the whole cohort.

As demonstrated in Table 2, retinal arteriolar caliber was significantly narrower in the Chinese (154.9 μm) than in the Malay (158.6 μm) and Indian (158.5 μm) children. Retinal venular caliber was also narrower in the Chinese (223.3μm) than in the Malay (230.8 μm) and Indian (229.0 μm) children. These differences were statistically significant, even after adjustments for age, gender, family income, parental education, body mass index, height, birth weight, axial length, and spherical equivalent ($P$ = 0.05 for arteriolar caliber; $P$ = 0.002 for

**TABLE 1.** Baseline Characteristics of Study Population

| Characteristic | N | Total n = 760 n | % | Chinese n = 654 n | % | Malay n = 75 n | % | Indian n = 31 n | % | P |
|---|---|---|---|---|---|---|---|---|---|---|
| Gender, male | 760 | 399 | 52.5 | 352 | 53.8 | 35 | 46.7 | 12 | 38.7 | 0.15 |
| Income | 736 | | | | | | | | | |
| ≤$2000/mo | | 202 | 27.4 | 142 | 22.5 | 50 | 67.6 | 10 | 33.3 | <0.001 |
| $2000–$5000/mo | | 305 | 41.4 | 264 | 41.7 | 24 | 32.4 | 17 | 56.7 | |
| >$5000/mo | | 229 | 31.1 | 226 | 35.8 | 0 | 0 | 3 | 10.0 | |
| Parental smoking, either parent smoked | 760 | 260 | 34.2 | 200 | 30.6 | 50 | 66.7 | 10 | 32.3 | <0.001 |
| Parental education, both no primary education | 760 | 108 | 14.2 | 82 | 12.5 | 21 | 28.0 | 5 | 16.1 | <0.001 |
| | | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | |
| Age (y) | 760 | 7.91 | 0.84 | 7.89 | 0.84 | 8.15 | 0.83 | 7.94 | 0.81 | 0.04 |
| Weight (kg) | 760 | 31.52 | 8.78 | 31.58 | 8.64 | 32.29 | 10.13 | 28.39 | 7.99 | 0.19 |
| Height (cm) | 760 | 135.0 | 9.7 | 135.2 | 9.8 | 134.6 | 9.4 | 132.5 | 9.2 | 0.29 |
| BMI (kg/m²) | 760 | 17.03 | 3.09 | 17.02 | 2.96 | 17.52 | 4.04 | 15.94 | 2.87 | 0.06 |
| BSA (m²) | 760 | 1.08 | 0.18 | 1.08 | 0.18 | 1.09 | 0.19 | 1.02 | 0.17 | 0.12 |
| Gestational age (wk) | 557 | 38.61 | 1.61 | 38.65 | 1.60 | 38.48 | 1.74 | 38.30 | 1.46 | 0.49 |
| Birth weight (g) | 751 | 3192 | 462 | 3201 | 460 | 3139 | 480 | 3123 | 473 | 0.39 |
| Birth length (cm) | 677 | 49.19 | 2.29 | 49.24 | 2.29 | 48.65 | 2.33 | 49.40 | 2.30 | 0.13 |
| Head circumference (cm) | 663 | 33.69 | 1.37 | 33.72 | 1.36 | 33.55 | 1.47 | 33.40 | 1.39 | 0.41 |
| Axial length (mm) | 760 | 24.21 | 1.02 | 24.24 | 1.01 | 24.26 | 0.92 | 23.36 | 1.12 | <0.001 |
| Spherical equivalent* | 760 | −2.00 | 2.39 | −2.03 | 2.5 | −2.00 | 1.16 | −1.08 | 2.00 | 0.29 |

Data are proportions or means and SD. *N,* number at risk; *n,* number with categorical endpoint.
* Data are median and interquartile range.

venular caliber). Differences in arteriolar caliber were not statistically significant in the model adjusted for MABP.

As Table 3 shows, retinal arteriolar and venular calibers were not significantly different between gender groups.

Similarly, birth factors, including birth weight, birth length, head circumference, and gestational age also were shown to have no consistent association with retinal vascular calibers (Table 4). Although in multivariate analysis adjusted for age, gender, and ethnicity, retinal venular caliber was 1.3 $\mu$m narrower for each standard deviation increase in birth weight (461 g; $P = 0.05$), this association was attenuated and lost its statistical significance after further adjustments for other potential confounders.

## DISCUSSION

The retinal vasculature provides a noninvasive window for the study of subtle small vessel changes. Our present study provides the first data on the distribution of retinal vascular caliber, as measured from digital fundus photographs with a validated technique, previously used only in adult populations, in a cohort of healthy school-aged children. Both retinal arterioles and venules were narrower in the Chinese children, compared with the Malay or Indian children, even after adjustment for age, gender, refraction, and other factors. However, we found, no consistent association of retinal vascular caliber with gender.

Another important observation in our study was the lack of association between retinal vascular caliber and various birth factors, including gestational age and birth weight. We had hypothesized that retinal vascular caliber may be related to various abnormal birth parameters, such as low birthweight, based on an increasing body of evidence that suggests a person's risk of cardiovascular diseases begins in early life. Studies have shown that abnormal fetal development, reflected by abnormal birth parameters such as low birth weight, is associated with an increased cardiovascular risk in adulthood, including risk of hypertension,[36,37] diabetes,[38,39] coronary heart disease,[40] and death.[22,41] However, these associations have not been consistently found in all studies, and the underlying

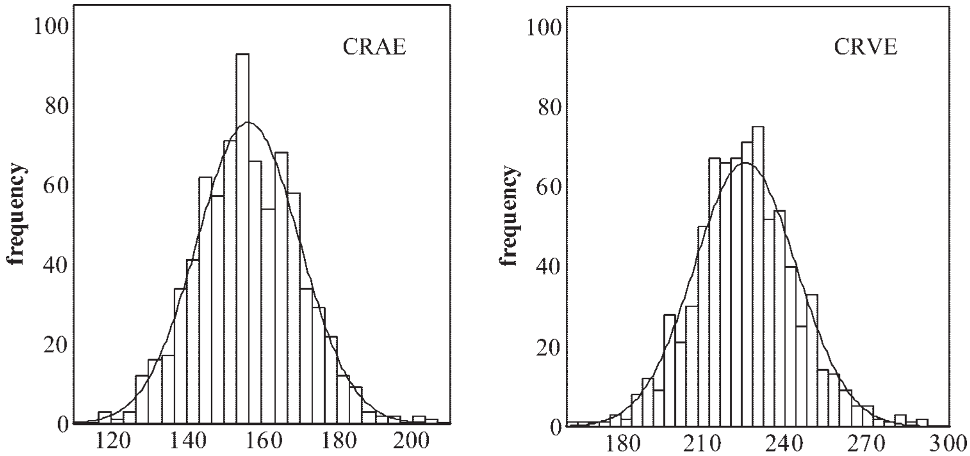


**FIGURE 1.** Distribution of CRAE (*left*) and CRVE (*right*), the Singapore Cohort study of the Risk factors for Myopia (SCORM).

**TABLE 2.** Relationship between Ethnicity and Retinal Vascular Caliber

| Ethnicity | N | Retinal Arteriolar Diameter (μm) Mean (95% CI) | P* | Retinal Venular Diameter (μm) Mean (95% CI) | P* |
|---|---|---|---|---|---|
| Model 1: adjusted for age, gender† | | | | | |
| All | 760 | 156.4 (155.4–157.3) | | 225.4 (224.1–226.8) | |
| Chinese | 654 | 155.8 (154.8–156.9) | 0.01 | 224.6 (223.2–226.1) | <0.001 |
| Malay | 75 | 158.7 (155.4–161.9) | | 231.5 (227.0–235.9) | |
| Indian | 31 | 162.5 (157.7–167.4) | | 236.3 (229.7–243.0) | |
| Model 2: multivariate adjusted‡ | | | | | |
| Chinese | 654 | 155.0 (153.5–156.4) | 0.01 | 223.2 (221.2–225.2) | <0.001 |
| Malay | 75 | 158.2 (154.8–161.5) | | 230.1 (225.5–234.7) | |
| Indian | 31 | 161.6 (156.6–166.7) | | 234.5 (227.6–241.3) | |
| Model 3: multivariate adjusted§ | | | | | |
| Chinese | 654 | 154.9 (153.5–156.3) | 0.05 | 223.3 (221.4–225.1) | 0.002 |
| Malay | 75 | 158.6 (155.3–161.8) | | 230.8 (226.5–235.1) | |
| Indian | 31 | 158.5 (153.6–163.4) | | 229.0 (222.5–235.5) | |
| Model 4: multivariate adjusted‖ | | | | | |
| Chinese | 355 | 154.3 (152.2–156.3) | 0.12 | 223.5 (220.7–226.3) | 0.02 |
| Malay | 11 | 161.5 (152.8–170.1) | | 240.5 (228.8–252.1) | |
| Indian | 14 | 159.2 (151.9–166.4) | | 227.5 (217.7–237.3) | |

Data are the mean and 95% CI.
* Comparison between ethnicities.
† Model 1: adjusted for age, gender, family income, and parental education.
‡ Model 2: model 1 plus BMI, height, and birth weight.
§ Model 3: model 2 plus axial length and spherical equivalent.
‖ Model 4: model 3 plus MABP.

mechanisms remain undefined.[42–44] The link between abnormal birth weight and subsequent cardiovascular disease, diabetes, and hypertension has been hypothesized to be related to small vessel disease.[45–48] Our study did not find an association between abnormal birth parameters and retinal vascular caliber in children.

We are unaware of any directly comparable studies of retinal vascular caliber in children, but other morphologic alterations of the retinal microvasculature have been evaluated and associated with lower birth weight, lower gestational age, and preterm birth.[10,11,13,18,49,50] For example, a population-based study has demonstrated an association of preterm birth with increased tortuosity of retinal vessels, independent of a previous history of retinopathy of prematurity.[13] It has also been shown that adults with a history of low birth weight or preterm birth have fewer retinal vascular branching points than do those with normal birth.[11] Moreover, a recent study of infants reported that increasing retinal temporal vascular angle may also be associated with preterm birth.[49] Apart from preterm birth, intrauterine growth restriction has also been related with narrower retinal arteriolar bifurcation angle[10] and reduced vascular branching points.[50] Although the actual underlying mechanisms of these observations are unclear, structural changes in the retinal microvasculature may be related to several biological processes.[51–53] It has been hypothesized that the abnormal retinal vascular pattern in preterm children reflects more widely spread vascular damage.[18] Some of the structural alterations studied (e.g., narrower arteriolar angle) have been linked with impaired mechanical efficiency of the general vascular network in the body, leading to greater work-

**TABLE 3.** Relationship between Gender and Retinal Vascular Caliber

| Gender | N | Retinal Arteriolar Diameter (μm) Mean (95% CI) | P* | Retinal Venular Diameter (μm) Mean (95% CI) | P* |
|---|---|---|---|---|---|
| Model 1: adjusted for age, ethnicity† | | | | | |
| Boys | 399 | 158.0 (155.8–160.3) | 0.05 | 229.7 (226.6–232.8) | 0.09 |
| Girls | 361 | 160.0 (157.8–162.1) | | 232.0 (229.0–235.0) | |
| Model 2: multivariate adjusted‡ | | | | | |
| Boys | 399 | 157.3 (154.9–159.8) | 0.07 | 228.0 (224.6–231.3) | 0.06 |
| Girls | 361 | 159.2 (156.8–161.6) | | 230.6 (227.3–233.8) | |
| Model 3: multivariate adjusted§ | | | | | |
| Boys | 399 | 157.7 (155.3–160.0) | 0.55 | 228.6 (225.5–231.8) | 0.18 |
| Girls | 361 | 157.0 (154.7–159.4) | | 226.7 (223.6–229.9) | |
| Model 4: multivariate adjusted‖ | | | | | |
| Boys | 214 | 159.0 (154.8–163.2) | 0.35 | 231.4 (225.8–237.1) | 0.36 |
| Girls | 166 | 157.6 (153.1–162.0) | | 229.5 (223.5–235.6) | |

Data are the mean and 95% CI.
* Comparison between gender.
† Model 1: adjusted for age, ethnicity, family income, and parental education.
‡ Model 2: model 1 plus BMI, height, and birth weight.
§ Model 3: model 2 plus axial length and spherical equivalent.
‖ Model 4: model 3 plus MABP.

**Table 4.** Relationship between Birth Factors and Retinal Vascular Caliber

| | Retinal Arteriolar Caliber (μm) | | Retinal Venular Caliber (μm) | |
|---|---|---|---|---|
| | Mean Difference (95% CI) | *P* | Mean Difference (95% CI) | *P* |
| Birth weight per SD (461 g) increase | | | | |
| Age and gender adjusted, model 1* | −0.06 (−1.03–0.90) | 0.90 | −1.30 (−2.62–0.02) | 0.05 |
| Multivariate-adjusted, model 2† | 0.44 (−0.53–1.41) | 0.37 | −0.78 (−2.08–0.51) | 0.24 |
| Multivariate-adjusted, model 3‡ | 1.06 (−0.38–2.51) | 0.15 | 0.31 (−1.67–2.28) | 0.76 |
| Gestational age per SD (1.61 weeks) increase | | | | |
| Age and gender adjusted, model 1* | 0.91 (−0.24–2.07) | 0.12 | −0.35 (−1.93–1.23) | 0.66 |
| Multivariate-adjusted, model 2† | 0.98 (−0.18–2.13) | 0.10 | −0.16 (−1.68–1.37) | 0.84 |
| Multivariate-adjusted, model 3‡ | 0.84 (−0.92–2.60) | 0.35 | 0.90 (−1.42–3.23) | 0.45 |
| Birth length per SD (2.30 cm) increase | | | | |
| Age and gender adjusted, model 1* | 0.03 (−0.99–1.05) | 0.96 | −0.96 (−2.36–0.44) | 0.18 |
| Multivariate-adjusted, model 2† | 0.55 (−0.46–1.57) | 0.28 | −0.38 (−1.74–0.98) | 0.59 |
| Multivariate-adjusted, model 3‡ | −0.29 (−1.75–1.17) | 0.70 | 0.02 (−1.98–2.02) | 0.99 |
| Head circumference per SD (1.38 cm) increase | | | | |
| Age and gender adjusted, model 1* | −0.10 (−1.14–0.95) | 0.86 | −0.68 (2.12–0.75) | 0.35 |
| Multivariate-adjusted, model 2† | 0.63 (−0.42–1.67) | 0.24 | −0.06 (−1.47–1.34) | 0.93 |
| Multivariate-adjusted, model 3‡ | 1.33 (−0.17–2.83) | 0.08 | 1.29 (−0.79–3.36) | 0.22 |

* Adjusted for age, gender and ethnicity.

† Adjusted for age, gender, ethnicity, parental education, axial length, spherical equivalent, height, BMI, birth weight, and family income.

‡ Adjusted for age, gender, ethnicity, parental education, axial length, spherical equivalent, height, BMI, birth weight, family income, and MABP.

load on the cardiovascular system and subsequent increase in risk of cardiovascular disease development.[10] The collective data from these studies underscore the importance of assessing architectural changes in the retinal vascular network in children. Our present study, nevertheless, showed no association between retinal vascular calibers and a range of birth factors including gestational age and birth weight. It is possible that retinal vascular caliber may only reflect cumulative effects of systemic insults, and therefore retinal vascular caliber changes may not manifest at an early stage in life.

The principal significant finding in our study is the ethnic differences in retinal vascular caliber, in which, Chinese children appeared to have narrower retinal vessels. We showed that the ethnic differences are evident even among Asian ethnic groups in the same country. However, the lack of data in the current literature leaves this observation unsupported, and the biological mechanisms underlying this association remain uncertain. We propose several possibilities: First, the narrower retinal vascular calibers in Chinese children may be related to inherent biological differences due to dissimilar genetic make-up compared with other ethnic groups.[54] This is supported by a study in a multiethnic population of adults, showing that Chinese appear to have smaller retinal arterioles compared to some other ethnic–racial groups such as Hispanics or African Americans.[55] Further, smaller retinal vascular caliber may also be a result of ocular refraction. Previous studies have found an association between myopic refraction and narrower retinal arteriolar as well as venular calibers.[56] However, this is unlikely to account for our finding, because in our population, there was no significant difference in spherical equivalent between different ethnic groups; in addition, adjustments for both axial length and spherical equivalent had minimal impact on the overall results.

Our study data may have several potential research and clinical implications. First, the importance of studying topological variations of the retinal vasculature has gained increasing recognition.[57–59] Despite numerous studies of the retinal vascular caliber in adults, the reference data for this important vascular feature remains unclear as different population-based studies have shown different values. This may be related to reliability issues with the various algorithms used to calculate the retinal vascular caliber, the various prevalences of refractive errors in different populations, and most important, the inability to completely control for confounding effect from systemic (e.g., blood pressure, medication, diabetes, smoking) and ocular (e.g., glaucoma, diabetic retinopathy) disease processes in the adult populations. Our study represents the first attempt to provide reference data for the retinal vascular calibers in healthy school-aged children, which may be helpful in future studies of similar populations. Second, the data presented herein may also aid standardization in the field of retinal imaging for the purpose of cardiovascular stratification in young people with vascular risk factors such as hypertension. Increasing evidence suggests that even mildly elevated blood pressure can have an adverse effect on the vascular structure and function in asymptomatic young persons, and retinal examination may be useful in identifying retinal vascular changes in high-risk children.[60,61] Third, we found no association between retinal vascular calibers and birth parameters, indicating that adjusting for these factors in studies of retinal vascular calibers in children may not be crucial. In addition, this negative finding suggests that other retinal vascular characteristics, such as vascular tortuosity and branching angles, may be more sensitive markers for systemic insults related to abnormal birth. Last, the significant ethnic differences in retinal vascular calibers seen in our study confirm the need for adequate adjustment for ethnicity in future studies.

Strengths of our study include masked evaluation of retinal vascular caliber using a previously validated retinal imaging program and standardized ascertainment of potential confounders including anthropometric and ocular biometric factors. However, several potential limitations of our study merit consideration. First, unknown sources of variability cannot be excluded, and an error may have been introduced through the varied timing of retinal photography, since retinal vascular calibers may be influenced by "physiologic" variations in cardiac cycle[57] and autonomic nervous system activity.[58] Other possible methodological issues for retinal photography and measurement have been described elsewhere.[23] Second, although our study population was randomly selected from the SCORM cohort, the possibility of different associations in nonparticipants cannot be totally excluded. In addition, the school-based (three schools) design of our study may not be truly representative of the entire community. Last, since retinal vascular measurements were obtained several years after birth, whether changes in retinal vascular caliber at birth were related to birth factors remains as an open question.

In summary, we have described the distribution of retinal vascular caliber in a cohort of healthy school-aged children. In our study, the Chinese children had narrower retinal vessels than did the Malay or Indian children and retinal vascular caliber did not vary significantly with gender. Birth factors, including preterm birth, gestational age, and birth weight, were not found to be associated with changes in retinal vascular calibers in our study population. Because retinal vascular caliber is related to various cardiovascular and ocular diseases, it may be that ethnic variations in retinal vascular caliber should be taken into consideration in future studies.

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