Corneal Arcus and Its Associations with Ocular and General Parameters: The Central India Eye and Medical Study

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PURPOSE. To investigate the prevalence of corneal arcus and its associations.

METHODS. The Central India Eye and Medical Study was a population-based study performed in rural Central India on 4711 subjects (age, 30+ years). Corneal arcus was assessed in corneal photographs.

RESULTS. The study included 952 randomly selected participants. Mean body mass index (BMI) was 19.8 ± 3.6 kg/m², with 786 (41.3%) subjects being underweight (BMI < 18.5 kg/m²). Corneal arcus of any degree was detected in 102 (10.7% ± 1.0%; 95% CI, 8.8–12.7) subjects. Corneal arcus was significantly associated with increasing age (P < 0.001). It was not significantly (all P > 0.10) associated with serum concentrations of high-density lipoproteins, cholesterol, creatinine, glucose, and glycosylated hemoglobin; with prevalence of arterial hypertension and diabetes mellitus; with body height, weight, and BMI; or with level of education, daily activities, nutrition, alcohol consumption, smoking, and blood pressure. In an intereye comparison, corneal arcus was significantly more marked in the eye with lower intraocular pressure (P = 0.006), thinner central cornea (P = 0.005), and more hyperopic refractive error (P = 0.003).

CONCLUSIONS. In this adult rural Central Indian population with low mean BMI, the prevalence of corneal arcus was 10.7% ± 1.0%. The only systemic parameter associated with corneal arcus was increasing age (P < 0.001). Corneal arcus was not associated with dyslipidemia, diabetes mellitus, arterial hypertension, alcohol consumption, or smoking. In this population with low BMI, corneal arcus was not a clinical biomarker for major metabolic disorders. The intereye associations between corneal arcus and low intraocular pressure, thin central cornea, and hyperopia may be of importance in the ophthalmic examination. (Invest Ophthalmol Vis Sci. 2011;52:9636–9643) DOI:10.1167/iovs.11-8404

The corneal arcus is a whitish ringlike structure that is located in the periphery of the cornea in the stromal layers superiorly and inferiorly and is separated from the limbus by a clear zone, also called the lucid interval of Vogt. Since it can be simply assessed during any routine clinical examination, an easily visible corneal arcus has usually raised interest beyond ophthalmology. Previous population-based investigations and hospital-based studies have described that a corneal arcus is associated with older age, the male sex, increased blood lipid levels, the prevalence of dyslipoproteinemias including familial hypercholesterolemia, and the presence of atherosclerosis, coronary heart disease and cardiovascular disease mortality, and ocular hypotony. In the recent population-based Singapore Malay Eye Study on the urban Malay population of Singapore, the prevalence of corneal arcus was 57.9% in the population aged 40 to 80 years. In the previous Blue Mountains Eye Study of Australians older than 49 years, the overall prevalence of circumferential corneal arcus was 64.8%. In the Singapore Malay Eye Study and in the Blue Mountains Eye Study, the corneal arcus was assessed during a slit lamp examination. The corneal arcus has not been assessed in any other population investigation.

The corneal arcus is easily assessable during a general clinical examination performed by a nonophthalmologist, and it may have importance as a clinical biomarker for systemic abnormalities and diseases (such as dyslipidemias). A population-based study compared with hospital-based studies may have a better design for examining the prevalence and associations of a feature such as corneal arcus, and both previous population-based studies assessed the corneal arcus during slit lamp examination and not on photographs. For these reasons and because neither of these studies was performed on an Indian population group, we conducted the present study to analyze the frequency and correlations of the corneal arcus in a population-based investigation in Central India.

METHODS

The Central India Eye and Medical Study (CIEMS) was a population-based, cross-sectional study in Central India. As described recently in detail, the study was performed in eight villages in Kalmeshwar Tehsil, a rural region of Eastern Maharashtra approximately 40 km from Nagpur. The Medical Ethics Committee of the Medical Faculty Mannheim of the Ruprecht-Karls-University Heidelberg and a similar committee of the Suraj Eye Institute/Nagpur approved the study, and all participants gave informed consent, according to the Declaration of Helsinki. The villages were chosen as locations for the study because they are located in a typical rural region of Central India and are a relatively long distance from the nearest city (Nagpur). Of a total...
population of 13,606 villagers, 5,885 subjects met the inclusion crite-
ron of an age of 30+ years. There was no exclusion criterion. Of the
5,885 eligible subjects, 4,711 subjects (2191 men; 46.5%) participated,
resulting in a response rate of 80.1%. The mean age was 49.5±13.4
years (median, 47; range, 30–100), and the mean reported monthly
income was 1584 ±1235 rupees (1 U.S. dollar equals roughly 50
rupees); the rate of illiteracy was 35%. Of the 1174 nonparticipants,
685 (58.3%) were men; the mean age was 48.6 ±14.1 years (median,
45; range, 30–95). The group of study participants and the group of
nonparticipants did not differ significantly in age (P = 0.06), whereas
the proportion of men was significantly (P < 0.001) higher in the
group of nonparticipants.

All examinations were performed at the hospital. Trained social
workers filled out a questionnaire for the participants, which included
items regarding socioeconomic background and living conditions, to-
bacco use and alcohol consumption, and any known diagnosis of major
systemic diseases. The level of education was differentiated into il-
literacy, 1st to 5th grade, 6th to 8th grade, 9th to 12th grade, and
graduation or higher. In all subjects, the pulse, arterial blood pressure,
body height, weight, and results of a chest x-ray and an electrocardio-
gram were recorded. One-and-one-half hours after a standardized
lunch, blood and urine samples were obtained and biochemically
analyzed.

The study participants underwent a detailed ophthalmic examina-
tion, including testing of visual acuity by ophthalmologists or optomet-
rists. Uncorrected visual acuity and visual acuity with the subjects’
glasses and after refractive correction were measured using modified
Early Treatment of Diabetic Retinopathy Study (ETDRS) charts (Light
House Low Vision Products, New York, NY) at a distance of 4 m.
Automated refractometry and subjective refraction were performed on
all subjects independent of visual acuity. Keratometry was performed
with a nonautomatic kerometer (Appassawamy Assoc., Chennai, In-
da). Visual field examinations were performed with frequency-dou-
bbling perimetry using a screening program (C-20-1; Carl Zeiss Meditec,
Dublin, CA). Intraocular pressure was measured by a slit lamp-
mounted Goldmann application tonometer. If the measurements were
higher than 21 mm Hg, tonometry was repeated. Slit lamp biomicros-
copy was performed by a fellowship-trained ophthalmologist, and any
anomaly of the anterior segment was noted. Gonioscopy was per-
formed for all study participants in dim illumination using the magna
view single mirror gonio lens (Ocular Instruments, Bellevue, WA). The
pupil was dilated, and a second slit lamp examination was performed
to assess the presence of pseudoexfoliation of the lens. Digital photo-
graphs of the cornea and lens were taken. Using the corneal photo-
ographs, corneal arcus was semiquantified in a masked fashion into six
grades with 0 indicating no corneal arcus and 5 indicating maximum
corneal arcus. The examination of the corneal arcus was performed by
a trained examiner (SV) assisted by two clinicians (SPJ, JBJ). The lens
nuclear sclerosis was graded according to the Age-Related Eye Disease
Study. Digital monoscopic photographs of the optic disc (20°) and
of the disc and macula (50°) were also taken. Magnification by optic
media was corrected for by a built-in algorithm. The optic disc size was
measured by confocal laser scanning tomography (Heidelberg Engi-
neering Co., Heidelberg, Germany). With the subject supine, ocular
pachymetry and biometry were performed by ultrasonography (Pac-
scan; Sonomed, Bayamon, Puerto Rico). Central corneal thickness,
anterior chamber depth, lens thickness, and axial length were mea-
sured for both eyes of all subjects.

The corneal photographs were evaluated for a randomly selected
subgroup of subjects who were included in the study described herein.
Inclusion criterion was the availability of assessable corneal photo-
graphs. Corneal photographs were available for 9372 (99.5%) of the
9422 eyes. There were no exclusion criteria. Statistical analysis was
performed with a commercially available statistical software package
(SPSS for Windows, ver. 19.0; SPSS, Chicago, IL). In the analysis,
we first calculated the mean prevalence of the corneal arcus in the study
population. As a second step, we assessed the associations between
the amount of corneal arcus and other ocular and general parameters,
adjusted for age and sex. In the third step of the statistical analysis, we
performed a stepwise multivariate analysis with corneal arcus as de-
pendent parameter and all systemic variables as independent param-
ters for which the P value in the univariate analysis was ≤0.20. In
a fourth step of the multivariate analysis, we adjusted the data of the
corneal arcus for the systemic parameters that remained significantly
associated with corneal arcus and assessed the relationship with ocular
parameters. In an additional step of the statistical analysis, we exam-
ined intereye differences (right eye minus left eye) of the degree of
corneal arcus and correlated them with intereye differences (right eye
minus left eye) of other ocular parameters such as intraocular pressure.
Prevalence data are given as the mean ± SE; all other data are pre-
sented as the mean ± SD. Odds ratios (OR) and 95% confidence intervals (95% CI) are presented. All P values are two-sided and are
considered statistically significant when the values are <0.05.

RESULTS

Of the 4711 subjects (9422 eyes), corneal photographs of a study group of 1904 eyes of 952 randomly selected subjects were
examined. The subjects of the study group and the subjects of the remaining study population did not differ in age (49.3 ±13.0 years versus 49.5 ±13.5 years; P = 0.75), sex
(men/women: 443/509 vs. 1748/2011; P = 1.00), refractive
error (−0.08 ± 1.75 diopters versus −0.17 ± 1.81 D; P = 0.15), and level of education (1.3 ± 1.2 vs. 1.3 ± 1.3; P = 0.43).

Our study population showed a mean body mass index (BMI) of 19.8 ± 3.6 kg/m^2, with 34 (1.8%) subjects of the study population being obese (BMI ≥ 30 kg/m^2), 154 (7.0%) being
overweight (30 kg/m^2 > BMI ≥ 25 kg/m^2), and 786 (41.3%) being underweight (BMI < 18.5 kg/m^2). Among the latter, 210
(11.0%) subjects were severely thin (BMI < 16.0 kg/m^2). The mean
blood concentration of cholesterol was 179.5 ± 20.7 mg/dL; of high-density lipoproteins, 37.4 ± 9.7 mg/dL; and of
creatinine, 1.14 ± 1.12 mg/dL. Mean BMI significantly
decreased with age (P < 0.001; correlation coefficient, r = −0.13), whereas the concentrations of cholesterol (P = 0.28),
high-density lipoproteins (P = 0.62), and creatinine (P = 0.08) were
independent of age.

A corneal arcus of any grade was detected on the photo-
graphs of 102 (10.7%) subjects, with grade 1 detected in 61
(6.4%) subjects, grade 2 in 18 (1.9%) subjects, grade 3 in 10
(1.1%) subjects, grade 4 in 11 (1.2%) subjects, and grade 5 in 2
(0.2%) subjects. Its mean prevalence was 10.7% ± 1.0% (95% CI: 8.8, 12.7). In the study population with an age of 40+
years, the prevalence was 14.6% ± 0.9% (95% CI, 12.7–16.4),
and in the population with an age of 50+ years, the prevalence
was 20.5% ± 1.4% (95% CI, 17.8–23.2).

Since the prevalence of corneal arcus increased significantly
with age (P < 0.001) (Table 1; Fig. 1) and since the sex of the
subject, in general, is an important systemic parameter, the
assessment of associations between corneal arcus and other
parameters was adjusted for age and sex. After adjustment for
age and sex, prevalence of corneal arcus was significantly
associated with lower body height (P = 0.03), higher fre-
cency of vigorous activity during professional work (P = 0.03),
lower frequency of a moderately intensive professional
work (P = 0.02), less time spent walking or going by bicycle
(P = 0.03), more myopic refractive error (P = 0.02), and
shallower anterior chambers (Table 2). The prevalence of cor-
neal arcus was not significantly associated with diastolic or
systolic blood pressure; arterial hypertension; serum concen-
trations of high-density lipoproteins, cholesterol, creatinine,
glucose, or HbA1c; prevalence of diabetes mellitus; pack years
of smoking; or number of years of smoking; nutrition (number
fruit intakes [P = 0.96] and vegetable intakes); or corneal
refractive power, lens thickness, or axial length (Table 2).
### Table 1. Association between the Presence of a Corneal Arcus and Ocular and General Parameters by Univariate Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Corneal Arcus (n = 102)</th>
<th>No Corneal Arcus (n = 850)</th>
<th>P</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic Parameters</strong></td>
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<tr>
<td>Age, y</td>
<td>62.4 ± 11.3</td>
<td>47.7 ± 12.2</td>
<td>&lt;0.001</td>
<td>-14.7</td>
<td>-17.2 to -12.4</td>
</tr>
<tr>
<td>Men/women</td>
<td>47/55</td>
<td>396/454</td>
<td>1.00</td>
<td></td>
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</tr>
<tr>
<td>Body height, kg</td>
<td>154.1 ± 9.4</td>
<td>157.2 ± 9.1</td>
<td>0.002</td>
<td>3.16</td>
<td>1.22 to 5.10</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>45.5 ± 10.0</td>
<td>49.4 ± 10.9</td>
<td>&lt;0.001</td>
<td>3.92</td>
<td>1.83 to 6.00</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>19.0 ± 3.1</td>
<td>19.9 ± 3.7</td>
<td>0.01</td>
<td>0.86</td>
<td>0.20 to 1.52</td>
</tr>
<tr>
<td>Level education, 0–4</td>
<td>0.8 ± 1.0</td>
<td>1.4 ± 1.3</td>
<td>&lt;0.001</td>
<td>0.58</td>
<td>0.36 to 0.80</td>
</tr>
<tr>
<td>Mobile ownership, n (%)</td>
<td>0 (0)</td>
<td>16 (98)</td>
<td>0.40</td>
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<tr>
<td><strong>Daily Activity</strong></td>
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<tr>
<td>Minutes of working/day</td>
<td>404 ± 165</td>
<td>439 ± 131</td>
<td>0.08</td>
<td>35.2</td>
<td>3.3 to 67.1</td>
</tr>
<tr>
<td>Vigorous activity during work</td>
<td>17 (17)</td>
<td>311 (37)</td>
<td>&lt;0.001</td>
<td>-0.19</td>
<td>-0.29 to -0.10</td>
</tr>
<tr>
<td>Walking or cycling/week, min</td>
<td>51.9 ± 37.4</td>
<td>71.3 ± 53.2</td>
<td>&lt;0.001</td>
<td>19.4</td>
<td>10.6 to 28.2</td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
<td></td>
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<tr>
<td>How often fruits per week</td>
<td>0.9 ± 1.1</td>
<td>0.9 ± 1.1</td>
<td>0.96</td>
<td></td>
<td></td>
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<tr>
<td>How often vegetables/week</td>
<td>5.5 ± 1.4</td>
<td>5.3 ± 1.4</td>
<td>0.08</td>
<td>-0.25</td>
<td>-0.54 to 0.03</td>
</tr>
<tr>
<td><strong>Smoking and Alcohol Consumption</strong></td>
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<tr>
<td>Pack years</td>
<td>2.9 ± 10.8</td>
<td>3.0 ± 10.0</td>
<td>0.91</td>
<td></td>
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</tr>
<tr>
<td>Years of smoking</td>
<td>6.1 ± 15.2</td>
<td>5.1 ± 12.2</td>
<td>0.53</td>
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<tr>
<td>Alcohol consumed (never; monthly or less; 2–4 times/mo; 2–3 times/wk; 4+ times/wk; daily)</td>
<td>0.3 ± 0.8</td>
<td>0.6 ± 1.3</td>
<td>&lt;0.001</td>
<td>0.3</td>
<td>0.1 to 0.5</td>
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<tr>
<td><strong>Diabetes Mellitus</strong></td>
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<tr>
<td>Have diabetes, n (%)</td>
<td>6 (5.9)</td>
<td>48 (5.6)</td>
<td>0.82</td>
<td></td>
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<tr>
<td>Blood glucose concentration</td>
<td>129.2 ± 50.1</td>
<td>123.5 ± 31.4</td>
<td>0.26</td>
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<tr>
<td>Hb1AC</td>
<td>4.55 ± 0.96</td>
<td>4.48 ± 1.62</td>
<td>0.54</td>
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<tr>
<td><strong>Blood Pressure</strong></td>
<td></td>
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<tr>
<td>Arterial hypertension, n (%)</td>
<td>30 (29)</td>
<td>150 (18)</td>
<td>0.007</td>
<td>1.94</td>
<td>1.23 to 3.08</td>
</tr>
<tr>
<td>Systolic, mm Hg</td>
<td>131.1 ± 24.2</td>
<td>121.6 ± 19.3</td>
<td>&lt;0.001</td>
<td>-9.5</td>
<td>-14.4 to -4</td>
</tr>
<tr>
<td>Diastolic, mm Hg</td>
<td>74.2 ± 11.1</td>
<td>74.1 ± 12.7</td>
<td>0.92</td>
<td></td>
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<tr>
<td><strong>Serum Levels, mg/dL</strong></td>
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<tr>
<td>High-density lipoproteins</td>
<td>38.5 ± 13.7</td>
<td>37.3 ± 9.2</td>
<td>0.49</td>
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<tr>
<td>Cholesterol</td>
<td>179.6 ± 20.3</td>
<td>179.0 ± 25.7</td>
<td>0.82</td>
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<tr>
<td>Creatinine</td>
<td>1.13 ± 1.18</td>
<td>1.15 ± 0.41</td>
<td>0.74</td>
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<tr>
<td><strong>Ocular Parameters</strong></td>
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<tr>
<td>Corneal refractive power, D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Horizontal</td>
<td>44.6 ± 1.7</td>
<td>44.3 ± 1.7</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertical</td>
<td>44.5 ± 1.8</td>
<td>44.4 ± 1.6</td>
<td>0.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central corneal thickness, µm</td>
<td>507 ± 35</td>
<td>515 ± 33</td>
<td>0.02</td>
<td>8</td>
<td>1 to 15</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>3.15 ± 0.43</td>
<td>3.21 ± 0.30</td>
<td>0.15</td>
<td>0.07</td>
<td>-0.02 to 0.16</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>4.09 ± 0.62</td>
<td>4.05 ± 0.48</td>
<td>0.57</td>
<td></td>
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<tr>
<td>Axial length, mm</td>
<td>22.71 ± 0.93</td>
<td>22.67 ± 0.95</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractive error, D (spherical equivalent)</td>
<td>-0.47 ± 2.32</td>
<td>-0.03 ± 1.67</td>
<td>0.07</td>
<td>0.44</td>
<td>-0.03 to 0.91</td>
</tr>
<tr>
<td>Cylindrical refractive error, D</td>
<td>1.11 ± 1.11</td>
<td>0.78 ± 0.95</td>
<td>0.004</td>
<td>-0.33</td>
<td>-0.56 to -0.10</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>13.4 ± 3.0</td>
<td>13.8 ± 3.0</td>
<td>0.15</td>
<td>0.48</td>
<td>-0.15 to 1.10</td>
</tr>
</tbody>
</table>

*Education was categorized into five levels: 0, illiterate; 1, up to the 5th standard; 2, up to the 6th–8th standards; 3, up to the 9th–12th standards; and 4, graduation or higher.

In the third step of the statistical analysis, we performed a multiple regression analysis, with the presence of corneal arcus as the dependent parameter and the systemic parameters of age, sex, body height, body weight, and daily activity parameters (vigorous activity during work, moderately intensive work, and time spent walking or cycling). The associations of these parameters with the presence of corneal arcus had $P \leq 0.20$ in the analysis with adjustment for age and sex (Table 2). The analysis revealed that only age ($P < 0.001$) remained to be significantly associated with the presence of corneal arcus (Table 3).

In the fourth step of the statistical analysis, we adjusted the analysis for age (i.e., the one systemic parameter that was significantly associated with the presence of a corneal arcus) and sex and then searched for significant associations between the presence of corneal arcus and the ocular parameters (central corneal thickness, refractive error, and anterior chamber depth), for which $P$ was $\leq 0.20$ in the previous analysis (Table 2). The result showed that the presence of a corneal arcus was associated, in addition to age ($P < 0.001$), with a shallow anterior chamber depth ($P = 0.03$) and a more myopic refractive error ($P = 0.03$; Table 3). If the multivariate analysis included the presence of corneal arcus as the dependent variable and age, sex, BMI, and the serum concentrations of cholesterol, high-density lipoproteins, and creatinine as the independent variables, the serum concentrations were again not
significantly associated with corneal arcus (cholesterol: $P = 0.93$; OR, 1.00; 95% CI, 0.99–1.01; high-density lipoproteins: $P = 0.62$; OR, 1.01; 95% CI, 0.99–1.03; and creatinine: $P = 0.90$; OR, 1.02; 95% CI, 0.79–1.30).

If only subjects with blood concentrations of cholesterol of $\geq 180$ were included in the statistical analysis adjusted for age and sex, the presence of corneal arcus was again not significantly related to the concentrations of cholesterol ($P = 0.46$; OR, 1.01; 95% CI, 0.98–1.04).

In a fifth step of the statistical analysis, we compared the side differences (right minus left eye) in the presence and in the amount of corneal arcus with side differences in ocular parameters. We found that intereye differences in corneal arcus were significantly ($P = 0.01$) and negatively (correlation coefficient $r = -0.08$) associated with intereye differences in intraocular pressure: the lower the intraocular pressure, the higher the degree of corneal arcus (Fig. 2). In a similar manner, intereye differences in corneal arcus were significantly and negatively associated with intereye differences in central corneal thickness ($P = 0.008$; $r = -0.08$). Intereye differences in corneal arcus were not significantly associated with increasing age ($P = 0.001$) and more myopic refractive error ($P = 0.04$), whereas the amount of corneal arcus was not significantly ($P = 0.20$) associated with the intraocular pressure measurements. A similar result was obtained, if age was added to the multivariate analysis, thus confirming a previous assessment of the associations of intraocular pressure.

**DISCUSSION**

In the adult population of rural Central India, the prevalence of corneal arcus was 10.7 ± 1.0% (95% CI, 8.8–12.7). In univariate and multivariate analysis, corneal arcus was significantly associated with increasing age ($P < 0.001$). In multivariate analysis, corneal arcus was not significantly associated with serum concentrations of high-density lipoproteins, cholesterol, creatinine, glucose, and glycosylated hemoglobin, with the prevalence of arterial hypertension or diabetes mellitus, or with body height, weight, and BMI, level of education, daily activity, nutrition, alcohol consumption, smoking, and blood pressure. In an intereye comparison, asymmetry in corneal arcus was significantly associated with an inverse asymmetry in intraocular pressure and central corneal thickness and a positive asymmetry in refractive error.

The prevalence of corneal arcus found in our study was markedly lower than that reported in the two previous popu-
lation-based studies (Singapore Malay Eye Study: 57.9%; population aged 40–80 years,1 versus 14.6% ± 0.9%; 95% CI, 12.7–16.4 in the same age group in our study; Blue Mountains Eye Study: circumferential corneal arcus, 64.8%; population aged >49 years11 versus 20.5% ± 1.4%; 95% CI, 17.8–23.2, in the same age group in our study). The marked difference between our study and the two previous studies may not be fully explained by differences in the method (single slit lamp examination versus assessment on photographs with the possibility for repeated reassessments) or differences in ethnicity (urban Malay population, white Australian population, and rural Central Indians). In a clinical setting, it may be unusual to find a marked (i.e., circumferential) corneal arcus in most subjects examined, although the patients in an ophthalmology hospital are usually older than 50 years.

A major reason for the discrepancy between the Singapore Malay Study and the Blue Mountains Eye Study on one side and our study on the other side may be pronounced differences in the composition of the study population. The mean BMI was markedly lower in our rural study population (19.8 ± 3.6 kg/m²) than in the Singapore Malay Study population, with an average BMI of approximately 26.5 kg/m² and an approximate SD of 5.1 kg/m².15 In a parallel manner, the blood concentration of total cholesterol was lower in our study (179.5 ± 20.7

Table 2. Associations between Presence of Corneal Arcus and Ocular and General Parameters, Adjusted for Age and Sex

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
<th>OR</th>
<th>95% CI of OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body height, cm</td>
<td>0.03</td>
<td>0.97</td>
<td>0.95 to 0.99</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>0.12</td>
<td>0.99</td>
<td>0.99 to 1.01</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.36</td>
<td>0.98</td>
<td>0.94 to 1.03</td>
</tr>
<tr>
<td>Level of education, 0–4*</td>
<td>0.77</td>
<td>1.04</td>
<td>0.82 to 1.31</td>
</tr>
<tr>
<td><strong>Activities of Daily Living</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What is your working duration every day, in minutes?</td>
<td>0.92</td>
<td>1.00</td>
<td>1.00 to 1.00</td>
</tr>
<tr>
<td>Does your work involve mostly sitting or standing with &lt;10 minutes of walking at a same time? (yes/no)</td>
<td>0.28</td>
<td>0.72</td>
<td>0.40 to 1.30</td>
</tr>
<tr>
<td>Does your work involve vigorous activity for at least 10 minutes at a time? (yes/no)</td>
<td>0.05</td>
<td>1.95</td>
<td>1.06 to 3.49</td>
</tr>
<tr>
<td>On a typical day, how much time do you spend in vigorous work in minutes?</td>
<td>0.28</td>
<td>1.00</td>
<td>0.99 to 1.00</td>
</tr>
<tr>
<td>How many days a week do you do vigorous work?</td>
<td>0.55</td>
<td>0.91</td>
<td>0.68 to 1.23</td>
</tr>
<tr>
<td>Does your work involve moderate-intensity activity for at least 10 minutes at a time? (yes/no)</td>
<td>0.19</td>
<td>1.64</td>
<td>0.78 to 3.46</td>
</tr>
<tr>
<td>In a typical week, on how many days do you do moderate-intensity work?</td>
<td>0.02</td>
<td>0.77</td>
<td>0.62 to 0.95</td>
</tr>
<tr>
<td>How much time do you spend doing moderate-intensity work on a typical day, in minutes?</td>
<td>0.07</td>
<td>1.00</td>
<td>1.00 to 1.00</td>
</tr>
<tr>
<td>In a typical week, on how many days do you walk or bicycle for at least 10 minutes to get to and from places?</td>
<td>0.99</td>
<td>1.00</td>
<td>0.87 to 1.15</td>
</tr>
<tr>
<td>How much time do you spend walking/bicycling for travel in a day in minutes?</td>
<td>0.03</td>
<td>0.99</td>
<td>0.99 to 1.00</td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How consume vegetables/week?</td>
<td>0.34</td>
<td>0.93</td>
<td>0.80 to 1.09</td>
</tr>
<tr>
<td>How often fruits/week?</td>
<td>0.41</td>
<td>1.08</td>
<td>0.90 to 1.30</td>
</tr>
<tr>
<td><strong>Alcohol and Smoking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of alcohol consumption (never; monthly or less; monthly or less; 2–3 times/mo; 2–3 times/wk; 4+ times/wk; daily)</td>
<td>0.21</td>
<td>0.84</td>
<td>0.64 to 1.10</td>
</tr>
<tr>
<td>Pack years of smoking</td>
<td>0.34</td>
<td>0.99</td>
<td>0.97 to 1.01</td>
</tr>
<tr>
<td>Years of smoking</td>
<td>0.46</td>
<td>0.99</td>
<td>0.98 to 1.01</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic, mm Hg</td>
<td>0.35</td>
<td>1.01</td>
<td>0.99 to 1.02</td>
</tr>
<tr>
<td>Systolic, mm Hg</td>
<td>0.23</td>
<td>1.00</td>
<td>1.00 to 1.01</td>
</tr>
<tr>
<td>Arterial hypertension (yes/no)</td>
<td>0.75</td>
<td>1.05</td>
<td>0.74 to 1.52</td>
</tr>
<tr>
<td><strong>Serum Concentrations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High density lipoproteins, mg/dL</td>
<td>0.54</td>
<td>1.01</td>
<td>0.99 to 1.02</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>0.73</td>
<td>1.00</td>
<td>0.99 to 1.01</td>
</tr>
<tr>
<td>Cholesterol, per 10 mg/dL increase</td>
<td>0.89</td>
<td>0.99</td>
<td>0.88 to 1.12</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>0.72</td>
<td>1.00</td>
<td>0.99 to 1.01</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.89</td>
<td>1.00</td>
<td>0.99 to 1.01</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>0.37</td>
<td>1.00</td>
<td>1.00 to 1.01</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>0.87</td>
<td>0.99</td>
<td>0.86 to 1.14</td>
</tr>
<tr>
<td>Diabetes mellitus (yes/no)</td>
<td>0.58</td>
<td>0.82</td>
<td>0.41 to 1.06</td>
</tr>
<tr>
<td><strong>Ocular Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corneal refractive Power, D</td>
<td>0.23</td>
<td>0.94</td>
<td>0.86 to 1.04</td>
</tr>
<tr>
<td>Central corneal thickness, µm</td>
<td>0.20</td>
<td>1.00</td>
<td>0.99 to 1.00</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>0.03</td>
<td>0.60</td>
<td>0.38 to 0.95</td>
</tr>
<tr>
<td>Lens thickness</td>
<td>1.00</td>
<td>1.00</td>
<td>0.75 to 1.33</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>0.25</td>
<td>1.11</td>
<td>0.93 to 1.32</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.02</td>
<td>0.92</td>
<td>0.85 to 0.99</td>
</tr>
<tr>
<td>Cylindric refractive power, D</td>
<td>0.21</td>
<td>0.91</td>
<td>0.78 to 1.06</td>
</tr>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td>0.24</td>
<td>0.97</td>
<td>0.92 to 1.02</td>
</tr>
</tbody>
</table>

*Education was categorized into five levels: 0, illiterate; 1, up to the 5th standard; 2, up to the 6th–8th standards; 3, up to the 9th–12th standards; and 4, graduation or higher.
mg/dL or 4.7 ± 0.5 mmol/L) than in the Singapore Malay Study (~5.5 mmol/L). More important, the SD of 0.5 mmol/L in our study was half that in the Singapore Malay Study, approximately 1.1 mmol/L, so that the range of the cholesterol blood concentration was considerably smaller in our study population than it was in the Singapore Malay population. The smaller the range, the less likely one can find an association in statistical analysis, so that the Central India population may not have had a wide enough upper range for an effect to be evident.

Another important difference between the study populations was that, in our markedly rural population with a high prevalence of underweight (41.3%) and severe thinness (11.0%), BMI significantly (P < 0.001) decreased with increasing age, and the mean blood concentration of cholesterol did not change with age. Correspondingly, the prevalence of diabetes mellitus significantly increased from the age group of 30 to 40 years to the age group of 60 to 65 years and then significantly decreased toward the elderly age groups. This is in contrast to urban populations such as in Singapore and in Western countries such as Australia and may have been another reason why, in our study, in contrast to the Singapore Malay Study and Australian Blue Mountains Eye Study, the corneal arcus was not associated with hypercholesterolemia.

The finding that prevalence and degree of corneal arcus was not related to serum concentrations of lipids, glucose, Hb1Ac, and creatinine suggests that a corneal arcus was not a clinical biomarker for hyperlipidemia or other metabolic disorders in our rural study population. In the literature on urban populations or populations from Western countries, most studies reported on associations between the presence and amount of a corneal arcus and hyperlipidemia or diseases associated with hyperlipidemia. In the Framingham Heart Study data set, Fernandez et al. determined if corneal arcus was an independent risk factor for cardiovascular disease and coronary artery dis-

TABLE 3. Association by Multivariate Analysis between the Presence of Corneal Arcus and Ocular and General Parameters, Which Were Significantly Associated with the Prevalence of Corneal Arcus after Adjustment for Age and Sex

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
<th>OR</th>
<th>95% CI of OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>&lt;0.001</td>
<td>1.10</td>
<td>1.06 to 1.13</td>
</tr>
<tr>
<td>Sex</td>
<td>0.85</td>
<td>1.09</td>
<td>0.44 to 2.71</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>0.49</td>
<td>0.98</td>
<td>0.93 to 1.04</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>0.68</td>
<td>1.01</td>
<td>0.97 to 1.04</td>
</tr>
<tr>
<td>Does your work involve vigorous activity for at least 10 minutes at a time? (yes/no)</td>
<td>0.14</td>
<td>1.65</td>
<td>0.85 to 3.20</td>
</tr>
<tr>
<td>In a typical week, on how many days do you do moderate intensity activity?</td>
<td>0.26</td>
<td>3.83</td>
<td>0.38 to 38.7</td>
</tr>
<tr>
<td>How much time do you spend doing moderate intensity work on a typical day in minutes?</td>
<td>0.16</td>
<td>1.00</td>
<td>0.99 to 1.00</td>
</tr>
<tr>
<td><strong>Ocular Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central corneal thickness, μm</td>
<td>0.42</td>
<td>0.92</td>
<td>0.86 to 0.99</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>0.03</td>
<td>0.59</td>
<td>0.37 to 0.94</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.03</td>
<td>0.92</td>
<td>0.86 to 0.99</td>
</tr>
</tbody>
</table>

![Figure 2](https://example.com/fig2.png) The side difference (right eye minus left eye) in the degree of corneal arcus and in intraocular pressure in the Central India Eye and Medical Study.
ease. They performed a prospective analysis in the Framing-
ham Heart Study Original Cohort and Offspring Cohort data-
based including 23,376 patient examinations and identified
corneal arcus in 3,890 (17%) of which them. They found that
corneal arcus was a predictor of cardiovascular disease and
coronary artery disease at 4 and 8 years of follow-up (P <
0.0001). Corneal arcus, however, was no longer predictive of
either cardiovascular disease or coronary artery disease after
adjustment for age and sex at 4 and 8 years of follow-up (P >
0.05 for all). They concluded that a corneal arcus predicted
cardiovascular diseases and coronary artery disease in the com-
unity-based Framingham Heart Study cohort because of its
association with increasing age and that age was a potentially
confounding factor. Although the association between corneal
arcus and cardiovascular disease or coronary artery disease
after adjustment for age was not statistically significant, the
odds ratio of 1.07 and its confidence interval of 0.95 to 1.22
suggested a potential association. Correspondingly, the Blue
Mountains Eye Study found, after age adjustment, a significant
correlation between corneal arcus and higher concentrations
of total cholesterol over 5 mmol/L.11 The confidence intervals
of the odds ratio (1.0–5.2) of the odds ratio (2.3) for that association in the Blue
Mountains Eye Study overlapped with the confidence interval
in the Framingham Heart Study (0.95–1.22). As in our study,
corneal arcus was not associated with arterial hypertension or
smoking in the Blue Mountains Eye Study. In agreement with
the Blue Mountains Eye Study and the Framingham Heart
Study, the recent Singapore Malay Eye Study reported that,
adjusted for age by sex, total cholesterol, serum glucose,
and current smoking, cardiovascular risk factors were signifi-
cantly associated with corneal arcus.22 Other studies reporting
on associations between corneal arcus and dyslipidemias were
usually relatively small-scale, hospital-based studies on groups
of patients with selected diseases, such as familial hypercho-
lesterolemia, Tangier disease, or lecithin-cholesterol acyl trans-
ferase deficiency.4–9,13,15 since our study did not specifically
include patients with rare diseases, the findings of our study
cannot be taken as an assessment of relationships between a
corneal arcus and these rare disorders. Interestingly, the con-
fidence interval for the odds ratio of the association between corneal arcus and blood concentrations of cholesterol (mea-
sured in mmol/L) was 0.62 to 1.39 in our study (Table 2), and
this overlapped with the confidence intervals of the same odds
ratio in the Singapore Malay Study (1.1–1.3).

In an intereye comparison, a more marked corneal arcus
was significantly associated with lower intraocular pressure
(P = 0.006), thinner central cornea (P = 0.005), and more
hyperopic refractive error (P = 0.003; Table 3). These findings
partially confirm results from the Singapore Malay Eye Study, in
which after adjustment for age, sex, and systemic factors,
central corneal thickness was lower (P = 0.03) in eyes with
corneal arcus versus those without. In contrast to our study,
the Singapore Malay Eye Study found that a more marked
corneal arcus was significantly (P < 0.001) associated with
higher intraocular pressure.7 Also, in contrast to the Singapore
Malay Eye Study, our study showed the associations between
corneal arcus and central corneal thickness and intraocular
pressure in the assessment of intraindividual intereye asymme-
tries only, whereas in the interindividual analysis, corneal arcus
was associated only with central corneal thickness, but not
with intraocular pressure (Table 1). As a corollary, intraocular
pressure measurements obtained in our study correlated sig-
ificantly with higher central corneal thickness (P < 0.001) and
more myopic refractive error (P = 0.04), whereas the amount of corneal arcus was not significantly (P = 0.20)
associated with the intraocular pressure measurements in the
multivariate analysis. A similar result was obtained, if age was
added to the multivariate analysis. It may suggest that a corneal
arcus was of minor importance for the measurements of intra-
ocular pressure.

Interestingly, asymmetries in intraocular pressure were sig-
nificantly associated with asymmetries in corneal arcus (P =
0.01), but not with side differences in central corneal thickness
(P = 0.97) and refractive error (P = 0.90) in our study. It fits
with clinical descriptions on patients with marked unioocular
hypotony and a pronounced corneal arcus in the hypotonic
eye, and with descriptions of patients with unioocular elevated
intraocular pressure and a more pronounced corneal arcus in the
contralateral normotensive eye.9,21 The reasons for the
association between marked ocular hypotony and development
of a corneal arcus have remained unclear so far.

Smoking and alcohol consumption were not significantly
associated with corneal arcus in our study. This finding con-
trasts that in a report on the association between corneal arcus and alcoholism.22

Potential limitations of our study should be discussed. First,
a major concern in any prevalence study is nonparticipation.
The Central India Eye and Medical Study had a reasonably good
response rate (80.1%); however, differences between partici-
pants and nonparticipants can lead to a selection artifact.
Second, our study included only a randomly chosen subgroup
of subjects for whom the corneal photographs were examined.
This study group did, however, not differ from the remaining
study population in the major parameters of age, sex, level of
education, and refractive error. Third, our study included only
subjects residing in a purely rural region, a region that can be
considered to be markedly rural based on responses to the
questionnaire regarding socioeconomic background and life-
style. The study did not include subjects from an urban region,
so we can provide no information on any differences between
rural and urban regions with respect to the examined param-
eters and associations. Fourth, our study, as a cross-sectional
investigation, did not allow statements on the longitudinal
association between corneal arcus and age. Fifth, although the
described correlations with corneal arcus were statistically
significant, even if interdependencies between parameters
were taken into account in the multivariate analysis, one has to
discuss how clinically relevant they were. The relatively high
number of subjects included into the study might have allowed
findings to be statistically significant without clinical relevance.
Sixth, our study population was markedly different from the
study population from previous population-based investiga-

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### Table 4. Side Differences in the Degree of Corneal Arcus Associated with Side Differences in other Ocular Parameters in the Central India Eye and Medical Study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
<th>Regression Coefficient</th>
<th>95% CI</th>
<th>Standard Coefficient</th>
<th>Variance Inflation Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td>0.006</td>
<td>-0.016</td>
<td>-0.027 to -0.004</td>
<td>-0.089</td>
<td>1.00</td>
</tr>
<tr>
<td>Central corneal thickness, μm</td>
<td>0.005</td>
<td>-0.003</td>
<td>-0.004 to -0.001</td>
<td>-0.092</td>
<td>1.00</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.003</td>
<td>0.029</td>
<td>0.010 to 0.048</td>
<td>0.096</td>
<td>1.01</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>0.18</td>
<td>-0.050</td>
<td>-0.123 to 0.023</td>
<td>-0.044</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Data are the results of multivariate analysis.
tions addressing the prevalence and associations of corneal arcus. The markedly lower BMI and the markedly lower blood concentration of cholesterol in our study population with no large subgroups of study participants at the high end of the these parameters may have prevented us from finding a statistically significant association between the presence and amount of corneal arcus and high levels of cholesterol and the presence of dyslipidemia in our study. Seventh, the sensitivity and specificity of the corneal photographs for assessing corneal arcus was not examined. The strengths of our study include that first, the population size was relatively large; second, that the study population lived in rural villages in Central India where modern civilization had not had yet a marked influence on daily life and where a marked myopization had not yet occurred; and third, that in contrast to some previous population-based studies, persons with an age between 30 and 40 years were included.

In conclusion, in this adult rural Central Indian population with low mean BMI, the prevalence of corneal arcus was 10.7% ± 1.0%. The only systemic parameter tested and associated with corneal arcus was increasing age (P < 0.001). Corneal arcus was not associated with dyslipidemia, diabetes mellitus, or arterial hypertension or with alcohol consumption and smoking. In this population with low BMI and low mean blood concentrations of cholesterol, corneal arcus was not a clinical biomarker for major metabolic disorders. The intereye associations between corneal arcus and low intraocular pressure, thin central cornea, and hyperopia may be of importance in the ophthalmic examination.

References
