Journal of Health, Wellness and Community Research
ISSN: 3007, 0570

JHWCR

Type: Original Article
Published: 24 January 2026
Volume: IV, Issue: I
DOI: https://doi.org/10.61919/k7chq913

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Received 11, 10, 25
Accepted 21, 01, 2026

Authors' Contributions
Concept: SK, SA; Design: SK, SA; Data Collection: SK, SN, SABI, AS; Analysis: SK, SA; Drafting: SK, SA, SN

Declarations
No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Evaluation of the Association Between Axial Length and Cup-to-Disc Ratio Among Non-Glaucomatous Hypertensive Patients

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ABSTRACT

Background: *Cup-to-disc ratio (CDR) is a key clinical parameter for optic nerve head assessment, yet physiological variation may be influenced by ocular biometry and systemic factors such as hypertension. Axial length (AL) can modify optic disc morphology and may complicate interpretation of CDR during glaucoma screening in hypertensive patients without glaucoma.* ***Objective***: *To determine the association between axial length and cup-to-disc ratio among non-glaucomatous hypertensive patients.* ***Methods***: *An observational cross-sectional study was conducted on 94 hypertensive patients aged 18–70 years at Al-Shifa Eye Clinic, Ali Pur Chatha. Eligible participants had normal intraocular pressure (<21 mmHg) and AL between 21–26 mm. Blood pressure was assessed using a calibrated sphygmomanometer, AL was measured using A-scan ultrasonography, and vertical CDR was assessed by slit-lamp biomicroscopy with a +90D lens after dilation. Non-normality was assessed using the Kolmogorov–Smirnov test, and associations were evaluated using Spearman's correlation with multivariable linear regression adjusting for age.* ***Results***: *The cohort included 64 males (68.1%) and 30 females (31.9%), with mean age 42.19±15.71 years. Spearman's correlation showed no significant association between AL and CDR (OD: r=0.029, p=0.778; OS: r=0.135, p=0.195). In regression models, AL did not significantly predict CDR in either eye (OD: B=0.000, p=0.963; OS: B=0.011, p=0.097).* ***Conclusion:*** *Axial length was not significantly associated with cup-to-disc ratio in non-glaucomatous hypertensive patients within the studied biometric range*

Keywords

Hypertension; Cup-to-disc ratio; Axial length; Optic nerve head; Optic disc

INTRODUCTION

The optic nerve head represents a critical anatomical and functional site where retinal ganglion cell axons converge to form the optic nerve, and its structural integrity is routinely evaluated during ophthalmic examinations. Among the various optic disc parameters, the cup-to-disc ratio (CDR) remains one of the most widely used clinical indices for assessing optic nerve head morphology and for screening glaucomatous damage (1). Although CDR enlargement is classically associated with glaucoma, considerable physiological variation exists in non-glaucomatous individuals, influenced by demographic, ocular, and systemic factors (2). Population-based studies have demonstrated that the distribution of normal CDR varies across age groups and ethnicities, underscoring the importance of contextual interpretation rather than reliance on a fixed threshold (3).

Axial length is a fundamental biometric parameter of the eye and a major determinant of ocular size and refractive status. Variations in axial length are known to influence optic disc morphology by altering the spatial distribution of retinal nerve fibers and the biomechanical configuration of the optic nerve head (4). Eyes with longer axial length, particularly myopic eyes, often exhibit larger optic discs, peripapillary changes, and altered neuroretinal rim architecture, which may complicate the clinical assessment of CDR (5). Axial elongation predominantly occurs during early life, stabilizing in adulthood, with normal adult axial length typically ranging between 22 and 25 mm (6). Excessive axial elongation has been associated with structural retinal thinning and pathological changes that may mimic or mask optic neuropathies (7).

Beyond ocular biometrics, systemic conditions such as hypertension may independently affect optic nerve head appearance through microvascular and hemodynamic mechanisms. Hypertension is a well-established risk factor for cardiovascular disease and has been implicated in microvascular remodeling, including within the retinal and optic nerve circulation (8). Fundoscopic changes related to hypertension reflect cumulative microvascular damage and may influence optic disc perfusion and structure even in the absence of elevated intraocular pressure or overt glaucoma (9). Despite this, hypertensive patients without glaucoma are frequently underrepresented in studies examining optic disc morphology, leading to uncertainty regarding how systemic blood pressure may interact with ocular structural parameters.

Existing literature has explored the relationship between axial length and optic disc size in healthy populations, with several studies reporting a positive association between longer axial length and larger optic discs, as well as sex-based differences in disc morphology (10). However, the translation of these findings to clinical measures such as CDR remains inconsistent. Some population-based studies have identified associations between CDR and factors such as age, sex, intraocular pressure, and systemic blood pressure, while reporting minimal or no independent influence of axial length (11). Notably, these studies largely focus on general or healthy populations and do not specifically address individuals with systemic hypertension but normal intraocular pressure.

The lack of focused investigation in non-glaucomatous hypertensive patients represents an important knowledge gap. In clinical practice, hypertensive individuals often undergo optic disc evaluation for glaucoma screening, yet it remains unclear whether axial length meaningfully influences CDR in this subgroup or whether observed disc changes should be attributed primarily to systemic vascular factors. Clarifying this

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DOI: https://doi.org/10.61919/k7chq913

relationship is essential to avoid misclassification of physiological cupping as pathological and to improve the accuracy of optic nerve head assessment in hypertensive patients (12).

Therefore, the present study was designed to evaluate the association between axial length and cup-to-disc ratio in non-glaucomatous hypertensive adults with normal intraocular pressure. By isolating a hypertensive population and excluding glaucomatous and extreme refractive conditions, this study aims to provide clinically relevant evidence regarding whether axial length acts as a significant determinant of CDR in this specific context. The primary objective was to assess the correlation between axial length and CDR in both eyes of hypertensive patients, with the hypothesis that axial length would not demonstrate a significant association with CDR in the absence of glaucoma.

MATERIALS AND METHODS

This observational cross-sectional study was conducted to evaluate the association between axial length and cup-to-disc ratio among non-glaucomatous hypertensive adults. The cross-sectional design was selected as it allows for simultaneous assessment of ocular biometric parameters and optic nerve head characteristics within a defined population, facilitating estimation of associations without implying causality (13). The study was carried out at Al-Shifa Eye Clinic, Ali Pur Chatha, Pakistan, over a six-month period following formal synopsis approval.

Participants were recruited using a non-probability purposive sampling technique from patients attending the outpatient ophthalmology clinic. Adult patients aged 18 to 70 years with a documented diagnosis of systemic hypertension for at least one year were considered eligible. Hypertension status was confirmed through medical records and verified using standardized blood pressure measurements obtained with a calibrated sphygmomanometer, following established clinical guidelines (14). Only patients with normal intraocular pressure, defined as <21 mmHg measured by applanation tonometry, and axial length ranging from 21 to 26 mm were included. Exclusion criteria comprised a history or clinical evidence of glaucoma, ocular hypertension, optic nerve disease, retinal pathology affecting the optic disc, previous ocular surgery or trauma, extreme refractive errors, and any systemic or neurological condition known to affect optic nerve morphology.

Eligible patients were informed about the purpose, procedures, and voluntary nature of the study, and written informed consent was obtained prior to enrollment. Demographic information, including age and sex, was recorded at the time of recruitment. All participants underwent a comprehensive ophthalmic examination conducted by trained optometrists to ensure standardized data collection and minimize inter-observer variability.

Axial length measurements were obtained for both eyes using A-scan ultrasonography performed under standardized conditions. Care was taken to ensure proper alignment and minimal corneal compression during measurements to enhance accuracy and reproducibility, consistent with established biometric protocols (15). For each eye, multiple readings were acquired, and the average value was recorded for analysis. Cup-to-disc ratio was assessed through slit-lamp biomicroscopy using a +90 diopter lens after pharmacological pupillary dilation to allow optimal visualization of the optic nerve head. Vertical CDR was determined clinically by evaluating the ratio of the vertical diameter of the optic cup to that of the optic disc, as this parameter is considered more sensitive to early structural changes (16). Measurements for both eyes were documented independently using a structured data collection sheet.

The primary variables of interest were axial length (continuous variable, measured in millimeters) and cup-to-disc ratio (continuous variable). Age was treated as a potential confounding variable due to its known influence on optic nerve head morphology, while sex was considered as a covariate in exploratory analyses (17). To reduce measurement bias, all assessments were performed using standardized instruments and consistent examination protocols, and data entry was cross-checked for accuracy to ensure data integrity.

Sample size estimation was performed a priori using G*Power software to ensure adequate statistical power to detect a clinically meaningful correlation between axial length and CDR. The calculation was based on a two-tailed test for correlation, assuming a medium-to-large effect size, a significance level (α) of 0.05, and a statistical power of 80%, resulting in a required sample size of 94 participants. This sample size was deemed sufficient to allow stable estimation of correlation coefficients and regression parameters (18).

Statistical analysis was conducted using IBM SPSS Statistics software. Data were initially assessed for completeness and outliers prior to analysis. Normality of continuous variables was evaluated using the Kolmogorov–Smirnov test. As the data were not normally distributed, non-parametric methods were employed. Spearman's rank correlation coefficient was used to assess the association between axial length and cup-to-disc ratio separately for the right and left eyes. Multiple linear regression analyses were subsequently performed to evaluate whether axial length independently predicted CDR after adjusting for age, with separate models constructed for each eye. Regression assumptions, including linearity and absence of multicollinearity, were assessed prior to model interpretation. Statistical significance was defined as a p-value <0.05 with corresponding 95% confidence intervals reported where applicable (19).

The study protocol was reviewed and approved by the relevant institutional ethics committee, and all procedures adhered to the principles of the Declaration of Helsinki for research involving human participants (20). Participant confidentiality was maintained throughout the study by anonymizing data prior to analysis, and access to the dataset was restricted to the research team to ensure ethical compliance and reproducibility.

RESULTS

Table 1 summarizes the demographic profile of the 94 hypertensive, non-glaucomatous participants included in the analysis. The sample was predominantly male, with 64 males representing 68.1% of the cohort, while 30 participants were female (31.9%). The age ranged from 18 to 70 years, with a mean age of 42.19 years and a standard deviation of 15.71, indicating a relatively broad age distribution within the enrolled hypertensive population.

Table 2 presents the non-parametric association between axial length and cup-to-disc ratio (CDR) assessed using Spearman's rank correlation separately for each eye. In the right eye (OD), the correlation between axial length and CDR was negligible (Spearman's $r = 0.029$) and statistically non-significant ($p = 0.778$), with a 95% confidence interval spanning from −0.173 to 0.228, suggesting no meaningful directional relationship within the sampled range of axial length. In the left eye (OS), a weak positive correlation was observed ($r = 0.135$), but this association also did not reach statistical significance ($p = 0.195$). The corresponding 95% confidence interval (−0.070 to 0.326) crossed zero, reinforcing that the observed relationship could plausibly reflect random variation rather than a true association.

Table 3 details the multiple linear regression model predicting CDR in the right eye after adjustment for age. The overall model achieved statistical significance ($F(2, 91) = 2.970$, $p = 0.036$) and explained 9.0% of the variance in right-eye CDR ($R^2 = 0.090$; adjusted $R^2 = 0.060$). Despite the

DOI: https://doi.org/10.61919/k7chq913

overall model significance, neither predictor demonstrated an independent statistically significant effect. Axial length showed essentially no association with CDR (B = 0.000, SE = 0.009, β = −0.005, t = −0.047, p = 0.963), with a 95% confidence interval from −0.017 to 0.016, indicating a near-zero estimated change in CDR per 1-mm increase in axial length. Age also did not significantly predict right-eye CDR (B = 0.001, SE = 0.001, β = 0.129, t = 1.269, p = 0.208), with a 95% confidence interval of −0.001 to 0.003. The intercept was statistically significant (B = 0.474, p = 0.027; 95% CI: 0.055 to 0.893), reflecting the estimated baseline CDR when predictors are at zero, though this is not clinically interpretable given that age and axial length cannot realistically be zero.

Table 4 reports the analogous regression model for the left eye. Unlike the right eye, the overall model was not statistically significant (F(2, 91) = 2.490, p = 0.065) and explained 7.7% of variance in left-eye CDR ($R^2 = 0.077$; adjusted $R^2 = 0.046$). Axial length demonstrated a positive but non-significant association (B = 0.011, SE = 0.006, β = 0.171, t = 1.677, p = 0.097), with a 95% confidence interval ranging from −0.002 to 0.024, indicating that the estimated increase in CDR per 1-mm axial length increase could be as low as −0.002 or as high as 0.024 within sampling uncertainty. Age similarly showed no statistically significant effect on left-eye CDR (B = 0.001, SE = 0.001, β = 0.100, t = 0.975, p = 0.332), with a 95% confidence interval of −0.001 to 0.002. The intercept was also non-significant in the left-eye model (B = 0.152, p = 0.328; 95% CI: −0.155 to 0.459). Collectively, the correlation and regression outputs across Tables 2–4 consistently indicate that, within this hypertensive non-glaucomatous cohort, axial length was not significantly associated with cup-to-disc ratio in either eye.

A total of 94 non-glaucomatous hypertensive patients were included in the final analysis. Of these, 64 (68.1%) were male and 30 (31.9%) were female. The mean age of the participants was 42.19 ± 15.71 years, with an age range of 18 to 70 years. Detailed demographic characteristics of the study population are summarized in Table 1.

Table 1. Demographic characteristics of the study participants (n = 94)

Variable	Minimum	Maximum	Mean ± SD
Age (years)	18	70	42.19 ± 15.71

Sex	Frequency (n)	Percentage (%)
Male	64	68.1
Female	30	31.9
Total	94	100

Table 2. Association between axial length and cup-to-disc ratio using Spearman's correlation

Eye	Spearman's r	95% CI for r	p-value
Right eye (OD)	0.029	−0.173 to 0.228	0.778
Left eye (OS)	0.135	−0.070 to 0.326	0.195

Table 3. Multiple linear regression analysis predicting cup-to-disc ratio in the right eye (OD)

Predictor	B	SE (B)	β	t	p-value	95% CI for B
Constant	0.474	0.211	—	2.248	0.027	0.055 to 0.893
Axial length (mm)	0.000	0.009	−0.005	−0.047	0.963	−0.017 to 0.016
Age (years)	0.001	0.001	0.129	1.269	0.208	−0.001 to 0.003
Model statistics				Value		
F-statistic				F(2, 91) = 2.970		
R^2 / Adjusted R^2				0.090 / 0.060		
Model p-value				0.036		

Table 4. Multiple linear regression analysis predicting cup-to-disc ratio in the left eye (OS)

Predictor	B	SE (B)	β	t	p-value	95% CI for B
Constant	0.152	0.154	—	0.984	0.328	−0.155 to 0.459
Axial length (mm)	0.011	0.006	0.171	1.677	0.097	−0.002 to 0.024
Age (years)	0.001	0.001	0.100	0.975	0.332	−0.001 to 0.002
Model statistics				Value		
F-statistic				F(2, 91) = 2.490		
R^2 / Adjusted R^2				0.077 / 0.046		
Model p-value				0.065		

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DOI: https://doi.org/10.61919/k7chq913

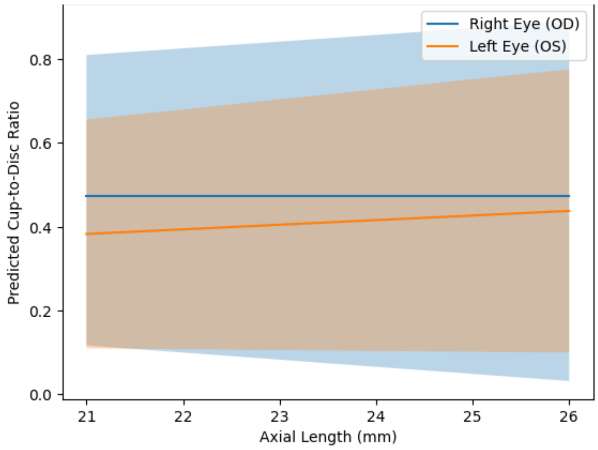

Figure 1 Modeled relationship between axial length and cup-to-disc ratio with 95% confidence bands in non-glaucomatous hypertensive patients

This figure illustrates the modeled association between axial length (21–26 mm) and predicted cup-to-disc ratio (CDR) for the right eye (OD) and left eye (OS), derived from the multivariable regression analyses. In the right eye, the predicted CDR remains essentially constant across the axial length spectrum, centered around 0.47, with a near-flat slope (B ≈ 0.000) and wide 95% confidence bands that expand modestly with increasing axial length, indicating minimal sensitivity of CDR to axial elongation. In contrast, the left eye demonstrates a shallow positive gradient, with predicted CDR increasing from approximately 0.38 at 21 mm to 0.44 at 26 mm, corresponding to the regression coefficient of 0.011 per millimeter; however, the broad confidence interval (−0.002 to 0.024 per mm) overlaps zero across the entire range. The substantial overlap of confidence bands between eyes and across axial lengths highlights the absence of a clinically meaningful or statistically robust axial length–CDR relationship in this hypertensive, non-glaucomatous cohort, reinforcing that observed inter-individual variability in CDR is unlikely to be explained by axial length alone.

DISCUSSION

The present study evaluated the association between axial length and cup-to-disc ratio in non-glaucomatous hypertensive adults with normal intraocular pressure and found no statistically significant correlation in either eye. Both non-parametric correlation analyses and multivariable regression models consistently demonstrated that axial length did not independently predict CDR after adjustment for age. These findings suggest that within a clinically typical axial length range, axial elongation alone does not substantially influence optic disc cupping in hypertensive patients without glaucoma.

The absence of a significant axial length–CDR relationship aligns with earlier work examining optic disc morphology in non-glaucomatous populations. Miglior et al. reported that while axial length was positively associated with optic disc size, it did not directly translate into proportional increases in cup-to-disc ratio, indicating that disc enlargement and cupping may represent distinct structural processes (21). This distinction is clinically relevant, as larger optic discs may physiologically accommodate larger cups without reflecting pathological neuroretinal rim loss. In the present study, restricting inclusion to individuals without glaucoma and extreme refractive errors likely reduced structural heterogeneity attributable to pathological remodeling, thereby clarifying the true magnitude of the axial length effect on CDR.

Large population-based studies further support the limited role of axial length in determining CDR. In the Shahroud Eye Cohort, vertical CDR was associated with age, sex, anterior chamber depth, and systemic factors such as hypertension, whereas axial length demonstrated only weak or inconsistent associations (22). Similarly, a nationwide Korean study involving over 28,000 healthy adults found that axial length did not exert a significant independent influence on CDR, while age, sex, intraocular pressure, and systemic vascular parameters showed more consistent effects (23). The current findings extend these observations to a hypertensive cohort, suggesting that systemic vascular status does not amplify the impact of axial length on optic disc cupping in the absence of glaucomatous pathology.

The regression analyses revealed that although the overall right-eye model achieved statistical significance, neither axial length nor age independently predicted CDR. This likely reflects the contribution of unmeasured factors, such as optic disc size, lamina cribrosa architecture, or microvascular perfusion, which collectively account for modest variability in CDR but were not directly assessed in this study. The shallow positive slope observed for axial length in the left eye, although not statistically significant, may represent random variation rather than a biologically meaningful trend, particularly given the wide confidence intervals overlapping zero. From a clinical standpoint, the magnitude of the estimated effect—approximately 0.01 change in CDR per millimeter of axial length—is unlikely to influence diagnostic decision-making.

Hypertension-related microvascular changes have been proposed as potential modifiers of optic nerve head morphology, raising concerns that systemic blood pressure may confound structural assessments used in glaucoma screening. However, the lack of a significant association between axial length and CDR in this hypertensive cohort suggests that axial elongation does not meaningfully distort CDR interpretation in patients with controlled hypertension and normal intraocular pressure. This finding is clinically reassuring, as it supports the continued use of CDR as a screening parameter in hypertensive patients without requiring routine adjustment for axial length within the normal biometric range.

An additional consideration is the method of CDR assessment. Clinical estimation using slit-lamp biomicroscopy, while widely used, may differ from imaging-based measurements. Zimmermann et al. demonstrated notable discrepancies between clinically assessed CDR and OCT-derived measurements, particularly in pediatric glaucoma suspects (24). Although OCT-based evaluation might provide greater precision, the consistency of findings across correlation and regression analyses in the present study suggests that any measurement variability was unlikely to obscure a clinically relevant association between axial length and CDR.

Several limitations should be acknowledged. The cross-sectional design precludes causal inference and does not account for longitudinal changes in axial length or optic nerve head morphology. The use of a single clinical setting and purposive sampling may limit generalizability. Additionally, analyzing both eyes independently does not fully account for inter-eye correlation, although similar patterns observed across eyes reduce concern for directional bias. Finally, optic disc size and vascular imaging parameters were not included, which may explain the relatively low proportion of explained variance in regression models.

Despite these limitations, the study has important strengths, including strict inclusion criteria excluding glaucomatous and extreme refractive conditions, standardized measurement protocols, and a focused hypertensive population that addresses a clinically relevant and underexplored subgroup. Collectively, the findings indicate that axial length does not significantly influence cup-to-disc ratio in non-glaucomatous hypertensive adults, supporting the interpretation of CDR as largely independent of axial length within this context. Future longitudinal studies incorporating optic disc size, vascular imaging, and advanced structural metrics may further elucidate the complex interactions between systemic health, ocular biometry, and optic nerve head morphology.

CONCLUSION

In conclusion, this study demonstrates that axial length is not significantly associated with cup-to-disc ratio in non-glaucomatous hypertensive adults with normal intraocular pressure. Both correlation and multivariable regression analyses consistently showed that variations in axial length within the clinically typical range do not meaningfully influence optic disc cupping, even in the presence of systemic hypertension. These findings suggest that cup-to-disc ratio can be interpreted without routine adjustment for axial length in hypertensive patients during glaucoma screening, thereby supporting its continued clinical utility. Further longitudinal and multimodal imaging studies are warranted to explore additional structural and vascular determinants of optic nerve head morphology in this population.

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