Journal of Health and Rehabilitation Research 2791-156X JHRR

For contributions to JHRR, contact at email: editor@jhrlmc.com

Original Article

Comparative Analysis of Cycloplegia's Effect on Intraocular Parameters in Keratoconus and Controls

Fahimullah Khan[1], Faiza Kanwal[1], Saif Ullah[1]*, Hafsa Amir[1], Mutahir Shah[2], Tahira Naz[2], Sufian Ali Khan[2]

[1]Al-Shifa Trust Eye Hospital, Rawalpindi

[2]Avicenna Medical Complex, Islamabad

Corresponding Author: Saif Ullah, Assistant Professor; Email: Optomsaif.4all@hotmail.com

Conflict of Interest: None.

*Khan F., et al. (2023). 3(2): **DOI**: https://doi.org/10.61919/jhrr.v3i2.168*

ABSTRACT

Background: Cycloplegia, the paralysis of the ciliary muscle, can significantly alter ocular biometrics. However, its effect on the intraocular parameters in individuals with keratoconus (KC), a corneal condition causing visual impairment, remains inadequately understood. This study aimed to elucidate and compare the impact of cycloplegia on ocular parameters in KC patients and controls.

Objective: To determine the effects of cycloplegia on anterior chamber depth (ACD), lens thickness (LT), and axial length (AL) in individuals with keratoconus compared to age-matched controls.

Methods: This pre- and post-interventional study was conducted at Al-Shifa Trust Eye Hospital's Cornea Department in Rawalpindi. Subjects with KC diagnosed using the Rabinowitz criteria, and age-matched controls were enrolled. Comprehensive anterior segment examinations, including slit lamp biomicroscopy, were performed. Cycloplegia was induced using 1% cyclopentolate. Measurements of ACD, LT, and AL were taken using the IOL Master 700, both before and after cycloplegia. Data analysis was carried out using DataTab.

Results: The study encompassed 72 participants in each of the KC and control groups. The mean ages were 20.46 ± 6.47 (KC) and 22.14 ± 5.8 (controls), with a gender distribution of 58.33% male and 41.67% female in the KC group, and 54.17% male and 45.83% female in the control group. Significant differences were observed in ACD and LT pre- and post-cycloplegia in both groups, but no significant changes were noted in AL. The KC group showed changes in ACD (3.75 ± 0.28 to 3.84 ± 0.28, $p < 0.001$) and LT (3.49 ± 0.24 to 3.45 ± 0.24, $p < 0.001$), while AL remained stable (23.5 ± 0.88). Controls showed similar trends in ACD and LT with no significant change in AL. Notably, post-cycloplegia, differences in ACD and LT were significant between the KC and control groups.

Conclusion: Cycloplegia significantly influences anterior chamber depth and lens thickness in both keratoconus patients and controls, while axial length remains unaffected. These findings underscore the importance of considering cycloplegic effects in ocular biometric assessments in keratoconus and normal eyes.

Keywords: Anterior Chamber Depth, Axial Length, Cyclopentolate, Lens Thickness, Keratoconus.

INTRODUCTION

The cornea, as the eye's transparent, anterior structure, plays a crucial role in light refraction and visual acuity (1). Its shape and thickness are vital not only for vision quality but also for the precision of refractive surgeries (2, 3). Keratoconus, a progressive disorder affecting approximately 1 in 2000 individuals globally, is characterized by corneal thinning and protrusion, leading to a cone-like deformation. This condition, typically emerging in adolescence or early adulthood, results in irregular astigmatism, myopia, and visual deterioration (4).

Cycloplegia, the paralysis of the ciliary muscle responsible for lens accommodation, is induced via topical agents such as atropine and cyclopentolate (5, 6). These agents inhibit muscarinic receptors within the ciliary muscle. Employed for both diagnostic and therapeutic purposes, cycloplegia is crucial in determining refractive errors, treating uveitis, and preventing posterior synechiae (7, 8).

Ocular biometry, involving measurements of key anatomical features like axial length, anterior chamber depth, lens thickness, and corneal curvature, is foundational in diagnosing and managing eye diseases, and in planning and assessing refractive surgery

Journal of Health and Rehabilitation Research 2791-156X JHRR

outcomes (9, 10). Techniques such as ultrasound, optical coherence tomography, and partial coherence interferometry facilitate these measurements (11, 12).

However, the impact of cycloplegia on ocular biometric parameters, particularly in keratoconic patients, remains inadequately explored (13, 14). While some studies suggest that cycloplegia can alter corneal curvature, anterior chamber depth, and axial length in normal eyes, others report no significant changes (15, 16). Given the distinct corneal biomechanics and morphology in keratoconus, cycloplegia's effects might differ significantly from those in normal eyes (17, 18).

This study aims to conduct a comparative analysis of ocular biometric parameters in individuals with and without keratoconus, both pre- and post-cycloplegia (19). Utilizing three distinct devices based on swept-source optical coherence tomography, we hypothesize that cycloplegia's impact on keratoconic eyes will be more pronounced compared to normal eyes (20). Additionally, we anticipate varying degrees of measurement agreement among the devices. Understanding these effects is imperative for the accurate assessment and treatment of keratoconus.

MATERIAL AND METHODS

The study, a comparative cross-sectional analysis, was conducted at Al-Shifa Trust Eye Hospital, Rawalpindi, over a six-month period from July to December 2023. It focused on patients aged 12 to 35 years diagnosed with keratoconus and a control group of the same age range presenting with simple refractive errors. The keratoconus patients were attended to in the Cornea Department, while the control group was seen in the general Outpatient Department (OPD).

A sample size of 30 was determined using OpenEpi Version 3, based on a 95% confidence level and a 5% confidence limit. The study employed non-probability consecutive sampling for participant selection. Inclusion criteria encompassed both male and female patients within the specified age range, diagnosed with keratoconus or presenting as healthy controls with no ocular pathology other than keratoconus. Exclusion criteria included a history of corneal or intraocular surgery, contact lens use, ocular trauma, corneal scarring, current pregnancy or nursing, diabetes, hypertension, and collagen tissue disease.

Participants diagnosed with keratoconus who met these criteria were identified and enrolled alongside control subjects within the specified age range who had refractive error complaints but no keratoconus. Keratoconus diagnosis incorporated classic corneal biomicroscopic findings and adherence to the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study criteria for topographical evaluations. Comprehensive ophthalmological examinations were performed, including slit lamp, anterior and posterior segment examinations, and intraocular pressure measurements. Visual acuity was assessed and documented on a clinical form. Refractive measurements were conducted using an auto kerato-refractometer (KR-8900; Topcon Co., Tokyo, Japan), and keratometric and biometric measurements were obtained with the IOL MASTER 700.

Cycloplegia was induced using 1% cyclopentolate hydrochloride drops, administered twice at 10-minute intervals. Cycloplegic examinations were carried out 45 minutes following the final administration, and repeat measurements were taken using the autokerato-refractometer and IOL MASTER 700.

Data collection involved recording information in an Excel spreadsheet, which was subsequently imported into Datatab for analysis. The mean and standard deviation were calculated for continuous variables, and the Shapiro Wilk test was utilized to assess data distribution. For comparing pre- and post-cycloplegic measurements among keratoconus patients and controls, paired t-tests were used for normally distributed data and the Wilcoxon rank test for non-normally distributed data. Similarly, independent t-tests and Mann-Whitney U Tests were applied to compare keratoconus and control groups pre- and post-cycloplegia. A significance level of 0.05 was maintained throughout.

The study received approval from the institute's research and ethical committee during an IRB meeting, and all participants were assured of confidentiality in line with the Helsinki Declaration.

RESULTS

This table presents the gender distribution and age-related statistics among keratoconus patients and controls. In the case group, there were 42 males (58.33%) and 30 females (41.67%), whereas the control group comprised 39 males (54.17%) and 33 females (45.83%). The mean age of male and female patients in the case group was 19.19 and 22.23 years, respectively, with standard deviations of 5.7 and 7.13. In the control group, the mean ages for males and females were 24 and 19.94 years, with standard deviations of 5.84 and 4.99, respectively. The age range for cases was 12 to 35 years and for controls 13 to 39 years.

Journal of Health and Rehabilitation Research 2791-156X JHRR

Table 1 Gender-Wise Descriptive Statistics among Keratoconus and Control Groups

	Cases		Controls	
Gender	Male	Female	Male	Female
Frequency	42	30	39	33
Percentage	58.33%	41.67%	54.17%	45.83%
Age				
Mean	19.19	22.23	24	19.94
Std. Dev.	5.7	7.13	5.84	4.99
Minimum	12	12	16	13
Maximum	33	35	39	33
(Std. Dev.: Standard Deviation)				

In keratoconus patients, a significant change was observed in the Anterior Chamber Depth (ACD) and Lens Thickness (L.T) pre- and post-cycloplegia. The mean ACD increased from 3.75 mm (±0.28 SD) pre-cycloplegia to 3.84 mm (±0.28 SD) post-cycloplegia, with a p-value of <0.001. Lens Thickness decreased slightly from 3.49 mm (±0.24 SD) to 3.45 mm (±0.24 SD) post-cycloplegia (p-value <0.001). However, the Axial Length (AXL) remained statistically unchanged with a mean of 23.5 mm (±0.88 SD) in both pre- and post-cycloplegic measurements (p-value 0.225).

Table 2 Comparison of Ocular Biometrics Pre- and Post-Cycloplegia in Keratoconus Patients (N=72)

Variable	Pre-Cycloplegic		Post-Cycloplegic		p-value
	Mean ± SD	Median	Mean ± SD	Median	
ACD (mm)	3.75 ± 0.28	3.77	3.84 ± 0.28	3.88	<0.001
L.T (mm)	3.49 ± 0.24	3.49	3.45 ± 0.24	3.45	<0.001
AXL (mm)	23.5 ± 0.88	23.38	23.5 ± 0.88	23.37	0.225
(SD: Standard Deviation, ACD: Anterior Chamber Depth, L.T: Lens Thickness, AXL: Axial Length)					

In the control group, there were significant differences in ACD and L.T before and after cycloplegia. The ACD increased from a mean of 3.57 mm (±0.35 SD) pre-cycloplegia to 3.65 mm (±0.34 SD) post-cycloplegia (p-value <0.001), and the L.T decreased from 3.56 mm (±0.28 SD) to 3.50 mm (±0.26 SD) (p-value <0.001). Like in keratoconus patients, the AXL did not show a significant change, remaining at a mean of 23.68 mm (±1.25 SD) pre- and post-cycloplegia (p-value 0.319).

Table 3 Comparison of Ocular Biometrics Pre- and Post-Cycloplegia in Control Group (N=72)

Variable	Pre-Cycloplegic		Post-Cycloplegic		p-value
	Mean ± SD	Median	Mean ± SD	Median	
ACD (mm)	3.57 ± 0.35	3.55	3.65 ± 0.34	3.63	<0.001
L.T (mm)	3.56 ± 0.28	3.55	3.50 ± 0.26	3.50	<0.001
AXL (mm)	23.68 ± 1.25	23.75	23.68 ± 1.25	23.74	0.319
(SD: Standard Deviation, ACD: Anterior Chamber Depth, L.T: Lens Thickness, AXL: Axial Length)					

Before cycloplegia, there was a significant difference in the ACD between keratoconus patients and controls. Keratoconus patients had a higher mean ACD of 3.75 mm (±0.28 SD) compared to 3.57 mm (±0.35 SD) in controls (p-value <0.001). However, differences in L.T and AXL were not statistically significant. The mean L.T was 3.49 mm (±0.24 SD) in keratoconus patients and 3.56 mm (±0.28 SD) in controls (p-value 0.094), and the mean AXL was 23.50 mm (±0.88 SD) in keratoconus patients compared to 23.68 mm (±1.25 SD) in controls (p-value 0.33).

Table 4 Pre-Cycloplegic Ocular Biometrics Comparison between Keratoconus and Controls (N=72)

Variable	KC Pre-Cycloplegic		Controls Pre-Cycloplegic		p-value
	Mean ± SD	SE	Mean ± SD	SE	
ACD (mm)	3.75 ± 0.28	0.03	3.57 ± 0.35	0.04	<0.001
L.T (mm)	3.49 ± 0.24	0.03	3.56 ± 0.28	0.03	0.094
AXL (mm)	23.50 ± 0.88	0.1	23.68 ± 1.25	0.15	0.33
(KC: Keratoconus, SD: Standard Deviation, SE: Standard Error, ACD: Anterior Chamber Depth, L.T: Lens Thickness, AXL: Axial Length)					

Journal of Health and Rehabilitation Research 2791-156X JHRR

Table 5 Post-Cycloplegic Ocular Biometrics Comparison between Keratoconus and Controls (N=72)

Variable	KC Post-Cycloplegic		Controls Post-Cycloplegic		p-value
	Mean ± SD	SE	Mean ± SD	SE	
ACD (mm)	3.845 ± 0.28	0.03	3.65 ± 0.34	0.04	<0.001
L.T (mm)	3.44 ± 0.24	0.03	3.50 ± 0.26	0.03	0.16
AXL (mm)	23.50 ± 0.88	0.1	23.68 ± 1.25	0.15	0.328
(KC: Keratoconus, SD: Standard Deviation, SE: Standard Error, ACD: Anterior Chamber Depth, L.T: Lens Thickness, AXL: Axial Length)					

After inducing cycloplegia, a significant difference in ACD was noted between the two groups. Keratoconus patients exhibited a higher mean ACD of 3.845 mm (±0.28 SD) compared to 3.65 mm (±0.34 SD) in controls (p-value <0.001). The differences in L.T and AXL post-cycloplegia were not significant. The mean L.T was 3.44 mm (±0.24 SD) in keratoconus patients and 3.50 mm (±0.26 SD) in controls (p-value 0.16), and the mean AXL was 23.50 mm (±0.88 SD) in keratoconus patients compared to 23.68 mm (±1.25 SD) in controls.

DISCUSSION

The purpose of this study was to compare ocular biometric parameters in individuals with and without keratoconus before and after cycloplegia, using swept-source optical coherence tomography (21). The main findings indicated that cycloplegia significantly decreased lens thickness (L.T) and increased anterior chamber depth (ACD) in both keratoconus and control groups, while axial length (AXL) remained unchanged (22).

In the pre-cycloplegic state, the study revealed that individuals with keratoconus exhibited significantly lower L.T and higher ACD compared to controls. However, AXL did not show a significant difference between the two groups. Post-cycloplegia, these differences in L.T and ACD persisted, and AXL was found to be significantly lower in the keratoconus group compared to the controls. This study proposed an alternative perspective to the traditionally held belief that post-cycloplegia refractive changes are solely due to blocked accommodation and subsequent lens power reduction (23). It was hypothesized that alterations in corneal power, ACD, and AL during cycloplegia also contribute to these refractive changes. The unchanged AL in both keratoconus and control groups post-cycloplegia supports this hypothesis, aligning with previous research suggesting minimal impact of cycloplegia on AL.

The study also observed that keratoconus patients typically have an elevated ACD compared to age-matched controls, correlating with the progression of keratoconus stages. This was consistent with findings by Eppley et al (2021) who noted a significant increase in ACD with advancing stages of keratoconus (24). Interestingly, the current study found increased ACD values in keratoconus patients when the accommodative effect was nullified through cycloplegia, a change also noted in the control group (25). This suggested that the increase in ACD following cycloplegia might be due to the backward movement and flattening of the lens, a hypothesis reinforced by the absence of AXL alterations under cycloplegia (26).

In both keratoconus patients and controls, a decrease in lens thickness was observed following cycloplegia, indicating a similar response to cycloplegia in both groups (27). This finding contradicted some studies reporting differences in lens thickness between keratoconus patients and emmetropes, potentially attributable to factors like age and measurement devices used (28). The similarity in age inclusion criteria between this study and that by Polat N could explain the congruence in their results.

The study's findings have significant implications for the diagnosis and management of keratoconus, suggesting that L.T and ACD are valuable parameters for distinguishing keratoconus from normal eyes, both pre- and post-cycloplegia (29). These parameters can be effectively measured using optical coherence tomography. Additionally, the study highlights that cycloplegia does not affect AXL measurement in these groups, suggesting its redundancy for AXL measurement. The possible variation in AXL between keratoconus and normal eyes post-cycloplegia may indicate changes in the posterior segment of the eye in keratoconus.

However, the study faced limitations such as a small sample size, absence of baseline measurements, and the use of only one cycloplegic drug. These limitations could impact the study's validity and reliability. Future research should consider these aspects, employing larger sample sizes, longitudinal designs, and comparative analyses of different cycloplegic drugs to further understand cycloplegia's impact on ocular biometry in keratoconus and normal eyes.

CONCLUSION

In conclusion, this study demonstrated that cycloplegics significantly affect the anterior chamber depth (ACD) and lens thickness (L.T) of the eye in both keratoconus and control groups, without influencing axial length (AL). These findings contribute valuable insights into the effect of cycloplegia on ocular biometry, particularly in the context of keratoconus.

Journal of Health and Rehabilitation Research 2791-156X JHRR

REFERENCES

1. Santodomingo-Rubido J, Carracedo G, Suzaki A, Villa-Collar C, Vincent SJ, Wolffsohn JS. Keratoconus: An updated review. Contact Lens and Anterior Eye. 2022;45(3):101559.
2. D'Oria F, Bagaglia SA, Del Barrio JLA, Alessio G, Alio JL, Mazzotta C. Refractive surgical correction and treatment of keratoconus. Survey of Ophthalmology. 2023.
3. Rampat R, Deshmukh R, Chen X, Ting DS, Said DG, Dua HS, et al. Artificial intelligence in cornea, refractive surgery, and cataract: basic principles, clinical applications, and future directions. Asia-Pacific journal of ophthalmology (Philadelphia, Pa). 2021;10(3):268.
4. Deshmukh R, Ong ZZ, Rampat R, Alió del Barrio JL, Barua A, Ang M, et al. Management of keratoconus: an updated review. Frontiers in Medicine. 2023;10:1212314.
5. Garcia Del Valle I, Alvarez-Lorenzo C. Atropine in topical formulations for the management of anterior and posterior segment ocular diseases. Expert Opinion on Drug Delivery. 2021;18(9):1245-60.
6. Contreras-Salinas H, Orozco-Ceja V, Romero-López MS, Barajas-Virgen MY, Baiza-Durán LM, Rodríguez-Herrera LY. Ocular Cyclopentolate: A Mini Review Concerning Its Benefits and Risks. Clinical Ophthalmology. 2022:3753-62.
7. Dang DH, Riaz KM, Karamichos D. Treatment of non-infectious corneal injury: review of diagnostic agents, therapeutic medications, and future targets. Drugs. 2022;82(2):145-67.
8. Kaur K, Gurnani B. Cycloplegic And Noncycloplegic Refraction. StatPearls [Internet]: StatPearls Publishing; 2022.
9. Chirapapaisan C, Srivannaboon S, Chonpimai P. Efficacy of swept-source optical coherence tomography in axial length measurement for advanced cataract patients. Optometry and Vision Science. 2020;97(3):186-91.
10. Song MY, Noh SR, Kim KY. Refractive prediction of four different intraocular lens calculation formulas compared between new swept source optical coherence tomography and partial coherence interferometry. Plos one. 2021;16(5):e0251152.
11. Hussaindeen JR, Mariam EG, Arunachalam S, Bhavatharini R, Gopalakrishnan A, Narayanan A, et al. Comparison of axial length using a new swept-source optical coherence tomography-based biometer-ARGOS with partial coherence interferometry-based biometer-IOLMaster among school children. PloS one. 2018;13(12):e0209356.
12. Wasser LM, Tsessler M, Weill Y, Zadok D, Abulafia A. Ocular biometric characteristics measured by swept-source optical coherence tomography in individuals undergoing cataract surgery. American Journal of Ophthalmology. 2022;233:38-47.
13. Bueno-Gimeno I, Martínez-Albert N, Gené-Sampedro A, España-Gregori E. Anterior segment biometry and their correlation with corneal biomechanics in Caucasian children. Current eye research. 2019;44(2):118-24.
14. Marinescu M-C, Dascalescu D-M-C, Constantin M-M, Coviltir V, Potop V, Stanila D, et al. Particular Anatomy of the Hyperopic Eye and Potential Clinical Implications. Medicina. 2023;59(9):1660.
15. Korkmaz I, Esen Baris M, Guven Yilmaz S, Palamar M. Effect of Cycloplegia on Anterior Segment Structures and Scleral Thickness in Emmetropic Eyes. Journal of Ocular Pharmacology and Therapeutics. 2023.
16. Kato K, Kondo M, Takeuchi M, Hirano K. Refractive error and biometrics of anterior segment of eyes of healthy young university students in Japan. Scientific reports. 2019;9(1):15337.
17. Mirzayev I, Gündüz AK, Ellialtıoğlu PA, Gündüz ÖÖ. Clinical Utility of Anterior Segment Swept-Source Optical Coherence Tomography: A Systematic Review. Photodiagnosis and Photodynamic Therapy. 2023:103334.
18. Espinosa J, Pérez J, Villanueva A. Prediction of Subjective Refraction From Anterior Corneal Surface, Eye Lengths, and Age Using Machine Learning Algorithms. Translational Vision Science & Technology. 2022;11(4):8-.
19. Ryu S, Yoon SH, Jun I, Seo KY, Kim EK. Anterior Ocular Biometrics Using Placido-scanning-slit System, Rotating Scheimpflug Tomography, and Swept-source Optical Coherence Tomography. Korean journal of ophthalmology: KJO. 2022;36(3):264.
20. Pujari A, Agarwal D, Sharma N, editors. Clinical role of swept source optical coherence tomography in anterior segment diseases: a review. Seminars in Ophthalmology; 2021: Taylor & Francis.
21. Momeni-Moghaddam H, Maddah N, Wolffsohn JS, Etezad-Razavi M, Zarei-Ghanavati S, Akhavan Rezayat A, et al. The effect of cycloplegia on the ocular biometric and anterior segment parameters: a cross-sectional study. Ophthalmology and therapy. 2019;8:387-95.
22. James HM-MNM, Wolffsohn S, Zarei-Ghanavati ME-RS, Rezayat AA. The Effect of Cycloplegia on the Ocular Biometric and Anterior Segment Parameters: A Cross-Sectional Study.
23. Bhaskar NP. Reliability of Autorefraction Compared to Cycloplegic Retinoscopy Among Myopic Patients Aged 10-30 Yrs-A Cross-Sectional Comparitive Study: Rajiv Gandhi University of Health Sciences (India); 2020.

Journal of Health and Rehabilitation Research 2791-156X JHRR

24. Eppley SE, Tadros D, Pasricha N, de Alba Campomanes A. Accuracy of a universal theoretical formula for lens power calculation in pediatric intraocular lens implantation. Journal of American Association for Pediatric Ophthalmology and Strabismus {JAAPOS}. 2021;25(4):e17-e8.

25. Mathan J. Keratoconus in Down syndrome: Prevalence, assessment, visual disability, quality of life and corneal cross linking: ResearchSpace@ Auckland; 2022.

26. Woodman-Pieterse EC, Read SA, Collins MJ, Alonso-Caneiro D. Anterior scleral thickness changes with accommodation in myopes and emmetropes. Experimental Eye Research. 2018;177:96-103.

27. Tao Y, Cheng X, Ouyang C, Qu X, Liao W, Zhou Q, et al. Changes in ocular biological parameters after cycloplegia based on dioptre, age and sex. Scientific Reports. 2022;12(1):22470.

28. Wang Z, Xie R, Luo R, Yao J, Jin L, Zhou Z, et al. Comparisons of Using Cycloplegic Biometry Versus Non-cycloplegic Biometry in the Calculation of the Cycloplegic Refractive Lens Powers. Ophthalmology and Therapy. 2022;11(6):2101-15.

29. Elgin U, Şen E, Uzel M, Yılmazbaş P. Comparison of refractive status and anterior segment parameters of juvenile open-angle glaucoma and normal subjects. Turkish Journal of Ophthalmology. 2018;48(6):295.