Central Corneal Thickness in Aphakic Children With Microcornea-Microphthalmia

Nader H.L. Bayoumi, MD and Nihal M. El Shakankiri, MD

Purpose: To study the central corneal thickness (CCT) in eyes with microcornea and aphakia and without glaucoma, compare it with normal controls, and correlate it with the measured intraocular pressure (IOP).

Methods: The study was conducted on 62 eyes of 31 aphakic children with microcornea. Controls (20 children) were selected from age-matched children presenting for routine refraction. Detailed anterior-segment and fundus examinations were conducted. The CCT and the axial length were measured. Medical records of the study patients were reviewed for the stability of the ocular parameters over time to exclude glaucoma.

Results: The mean ± SD age of the study patients and controls were 4.0 (± 3.1, 1.0 to 12.0) and 3.1 (± 2.7, 0.6 to 12.0) years, respectively. The mean ± SD CCT, the corneal diameter, the measured IOP, the cup/disc ratio, and the axial length of the study patients and the controls were 667.01 ± 72.90 μm, 8.9 ± 0.8 mm, 10.9 ± 5.7 mm Hg, 0.1 ± 0.1, 20.35 ± 2.90 mm and 545.22 ± 28.14 μm, 11.7 ± 0.5 mm, 5.3 ± 1.8 mm Hg, 0.1 ± 0.1, and N/A, respectively. The difference between the study eyes and the controls in the CCT and the measured IOP was statistically significant ($P < 0.05$).

Conclusions: Aphakic eyes with microcornea have thicker CCTs and greater measured IOPs than normal eyes. Hence, the measurement of CCT is recommended in the assessment of aphakic eyes with microcornea for possible glaucoma. The measured IOP, although a reliable parameter, in isolation does not provide a diagnosis of glaucoma and must be viewed in conjunction with other patient findings, such as the cup/disc ratio, the progression of which over time must be considered for a more solid diagnosis.

Key Words: children, glaucoma, aphakic, microcornea, microphthalmia, central corneal thickness

(*J Glaucoma* 2016;25:497–500)

Microcornea is a congenital ocular anomaly of the cornea in which the corneal diameter is < 10 mm.[1] Microcornea may occur as an isolated condition or it may be associated with a short axial length (AL) of the eye. It may also be associated with congenital cataract and/or glaucoma.[2–4] Congenital cataract surgery is reported to result in an increase in the central corneal thickness (CCT) in the operated eyes.[5] Congenital cataract surgery is also associated with a number of postoperative complications, significant among which is glaucoma, especially in the presence of other associated ocular anomalies, such as microphthalmia.[6,7] Measurement of the intraocular pressure (IOP) in children is an important part of the diagnosis of glaucoma after congenital cataract surgery. The effect of the CCT on the accuracy of IOP measurement, especially by applanation tonometry, has been reported.[8,9] It is generally known that thicker CCTs result in artifactually higher IOPs, and may subsequently result in an erroneous diagnosis of glaucoma. In addition, differences in CCTs of children among different ethnic groups have been reported.[9,10] The aim of the current study was to study the CCT in aphakic children with microcornea that were not glaucomatous, compare it with age-matched normal phakic eyes, and correlate it with the measured IOP by applanation tonometry.

METHODS

The study was conducted on 62 (31 right, 31 left) eyes of 31 (11 male, 20 female) aphakic children with microcornea, who presented to and were operated upon for congenital cataract in the Ophthalmology Department of Alexandria Main University Hospital in Alexandria, Egypt. The study was conducted in accordance with the Declaration of Helsinki in 1995, was granted approval by the ethics committee of the Faculty of Medicine of Alexandria University, and parents of the participating children provided approved consent for participation in the study. Cases with corneal edema and/or scarring, and cases diagnosed with or suspected of having glaucoma, were excluded from the study. Controls were selected from age-matched children presenting to the pediatric ophthalmology clinic of Alexandria Main University Hospital for checking the refraction. The children included as controls were examined in the office initially and were deemed to need examination under general anesthesia (GA) on account of their being uncooperative for a full thorough ophthalmic evaluation, including routine office refraction. For all study patients and controls, the same standard protocol was followed. An initial office examination was followed by an examination under GA. An initial assessment by a specialized pediatric anesthesiologist to assess for fitness for GA was followed by inhalational Sevoflourane (fluoromethyl hexafluoroisopropylether) anesthesia. Parameters assessed included the IOP using a Perkins tonometer, the horizontal white-to-white corneal diameter using calipers, anterior-segment examination using a portable slit lamp, and fundus examination using the indirect ophthalmoscope. Microcornea was diagnosed when the white-to-white corneal diameter was 9 mm or less till the age of 1 year or 10 mm or less at an older age.[11] The CCT was measured using the ultrasonic pachymeter (DGH Pachmate; DGH

Received for publication November 3, 2014; accepted August 11, 2015.
From the Ophthalmology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
This study was conducted in the Ophthalmology Department of Alexandria Main University Hospital, Alexandria Faculty of Medicine, Alexandria University, Egypt.
Disclosure: The authors declare no conflict of interest.
Reprints: Nader H.L. Bayoumi, MD, Ophthalmology Department, Faculty of Medicine, Alexandria University, 311 Horeya Avenue, Sporting, 10th Floor, App 1004, Alexandria, Egypt (e-mail: naderbayoumi@yahoo.com).

DOI: 10.1097/IJG.0000000000000323

Technology Inc., Exton, PA), which takes 25 serial measurements in rapid succession, then provides an average for the measurements. This was followed by measurement of the AL using A-scan ultrasonography (OTIScan2000; Ophthalmic Technologies Inc., Toronto, ON, Canada) for the study patients only and not the control eyes. As the main aim of this study was the CCT and the cornea, it was deemed unnecessary to obtain AL data from control eyes, thus helping minimize unnecessary manipulation of the control eyes. Being operated for cataract in the Ophthalmology Department of Alexandria Main University Hospital, the medical records of the study patients were reviewed for the stability of the ocular parameters over time to exclude the diagnosis of glaucoma. The average (range, median) interval from cataract surgery to the time of the examination included in the current study was 28 (7 to 54, 27) months. Glaucoma at the time of the study was excluded when the measured ocular parameters, namely the cup/disc ratio, AL, and refraction, were confirmed to be stable over that time period in the presence of serial IOP measurements in the same range as reported in the study for every eye. Nevertheless, it is obvious that glaucoma remains a lifelong risk for such eyes. The study eyes were then stratified according to the AL, in an attempt to isolate eyes with isolated microcornea and normal AL from eyes with microcornea and microphthalmia (short AL), with 21.0 mm[12] considered as the cutoff level. Data were tabulated and statistically analyzed.

Data were analyzed using the Statistical Package for Social Sciences (SPSS version 20; SPSS Inc., Chicago, IL). The distribution of quantitative variables was tested for normality using the Kolmogorov-Smirnov test, which revealed abnormal distribution of the data. Thus, nonparametric statistics were applied. Quantitative data were described using median, minimum, and maximum. Comparison of quantitative parameters between 2 groups was conducted using the Mann-Whitney *U* test. The correlation between quantitative parameters was determined using the Spearman ρ test. Comparison of categorical variables (sex and group) was performed using the χ^2 test. In all statistical tests, a level of significance of $P < 0.05$ was used, below which the results were considered to be statistically significant.

RESULTS

The study was conducted on a total of 51 children: 31 patients and 20 controls. Demographic data of the study patients and controls are shown in Table 1. The CCT of patients and controls and the rest of the clinical examination data and investigations are shown in Table 2. The difference in the CCT and the measured IOP between the study eyes and the control eyes was statistically significant ($P < 0.05$).

TABLE 1. Patient Demographics for All Study Patients

	Patients	Controls
Sex [n (%)]	31 (100)	20 (100)
Male	11 (64.5)	9 (55.0)
Female	20 (35.5)	11 (45.0)
Eyes [n (%)]	62 (100)	40 (100)
Right	31 (50)	20 (50)
Left	31 (50)	20 (50)
Age at examination (mean ± SD, range) (y)	4.0 (± 3.1, 1.0-12.0)	3.1 (± 2.7, 0.6-12.0)

TABLE 2. Clinical Examination Data for All Study Patients

	Mean ± SD (Range)	
	Patients	Controls
Central corneal thickness (μm)*	667.01 ± 72.90 (545-944)	545.22 ± 28.14 (506-623)
Corneal diameter (mm)	8.9 ± 0.8 (7-10)	11.7 ± 0.5 (11-12)
Measured intraocular pressure (mm Hg)*	10.9 ± 5.7 (3-32)	5.3 ± 1.8 (2-8)
Cup/disc ratio	0.1 ± 0.1 (0-0.5)	0.1 ± 0.1 (0-0.3)
Axial length (mm)	20.35 ± 2.90 (14.56-25.98)	N/A

*Statistically significant.

Demographic and Clinical Correlations for All (Patients and Controls) Study Eyes

Analysis of the correlation between the different study parameters revealed a statistically significant positive correlation between the age and both the IOP ($P = 0.003$) and the AL ($P = 0.000$), between the CCT and the IOP ($P = 0.000$), between the corneal diameter and the IOP ($P = 0.035$), and between the cup/disc ratio and the IOP ($P = 0.042$). There was no statistically significant correlation between the CCT and the AL ($P = 0.566$).

Demographic and Clinical Characteristics of Patients

Table 3 shows the demographic data of the study patients stratified according to the AL, and Table 4 shows the CCT and the rest of the clinical examination data and investigations for the same groups of study patients. The CCT did not show a statistically significant difference between these 2 groups of study eyes.

Eyes With Microcornea and Microphthalmia

For eyes with a short AL (< 21.0 mm, microphthalmic eyes), the difference in the CCT between the study eyes and the control eyes was statistically significant ($P < 0.05$).

Analysis of the correlation between the different study parameters revealed a statistically significant positive correlation between the age and both the IOP ($P = 0.029$) and the AL ($P = 0.001$), and between the CCT and both the IOP ($P = 0.029$) and the AL ($P = 0.007$).

Eyes With Isolated Microcornea (Normal AL)

For eyes with a normal AL (> 21.0 mm), the difference in the CCT between the study eyes and the control eyes was statistically significant ($P < 0.05$). Analysis of the correlation between the different study parameters revealed a statistically significant correlation between the CCT and each of the corneal diameter (this being a negative correlation, -0.406, $P = 0.049$) and the AL ($P = 0.001$), between the AL and the IOP ($P = 0.013$), and between the cup/disc ratio and the IOP ($P = 0.005$). Only the age showed a statistically significant difference between study eyes with normal and short AL ($P = 0.003$).

DISCUSSION

This study examined the CCT in nonglaucomatous aphakic children with microcornea/microphthalmia. There

TABLE 3. Patient Demographics for Short and Normal Axial Length (AL) Eyes

	Patients With AL < 21.0 mm	Patients With AL > 21.0 mm
Sex [n (%)]	20 (100)	13 (100)
Male	6 (30.0)	7 (53.8)
Female	14 (70.0)	6 (46.2)
Eyes [n (%)]	38 (100)	24 (100)
Right	20 (53)	11 (46)
Left	18 (47)	13 (54)
Age at examination (mean ± SD, range) (y)*	3.2 (± 2.6, 1.0-11.0)	5.3 (± 3.3, 2.0-12.0)

*Statistically significant.

is a paucity of the literature addressing the issue of CCT in eyes with microcornea-microphthalmia, and, to the best of the authors' knowledge , this is the first report on this issue in children in the Middle East. There was no statistically significant difference between the study eyes and the controls in their age or sex; hence, the sample was homogenous and the controls were selected adequately. The CCT was found to be significantly greater in eyes with microcornea than in normal controls. Likewise, the IOP measured was significantly higher in eyes with microcornea than in normal controls; yet, long-term follow-up of the study eyes confirmed that these eyes were not glaucomatous. The average CCT of 667 μm reported by the current study was a little greater than that reported by Filous et al[13] studying the same issue. Nevertheless, both studies along with other reports[14] highlight the effect of CCT on IOP measurement in this subset of children with small corneas and emphasize the notion that the diagnosis of glaucoma based on IOP measurement alone would likely to be faulty. As emphasized by previous studies,[15] other parameters, such as the cup/disc ratio or AL, should be utilized to make the diagnosis of glaucoma, especially when these show progression over time. In addition, both studies, the current study and that by Filous and colleagues, report a CCT in aphakic children with microcornea that is greater than that reported for aphakic children with normal corneal diameters,[5,16,17] providing additional emphasis that extra caution has to be exercised in such eyes with small corneas.

The current study also highlights a significant positive correlation between the age and the IOP, and this is in agreement with other studies supporting the fact that the IOP in very young children is lesser than that in older children and that the IOP normally increases to the normal adult level with time.[18] The fact that age and AL correlate significantly is well documented for normal eyes, wherein AL growth occurs maximally in the first 2 years of life. It is interesting to report the same trend in eyes with small corneas, hence demonstrating that the developmental anomaly resulting in the small cornea may not necessarily hinder normal elongation and growth of the eye. The fact that CCT correlates significantly with the IOP is just a confirmation of the already well-documented effect of CCT on IOP measurement.[8,9] It is interesting to note that in this study, there is a positive correlation between the cup/disc ratio and the IOP, even though these eyes were not glaucomatous at the time of conducting the study, with a reasonable postoperative follow-up time period.

When eyes with isolated microcornea and normal AL were studied alone, a significant negative correlation appears between the corneal diameter and the CCT, a fact previously reported in eyes with various types of childhood glaucoma.[19] In the same subgroup of patients, namely those with microcornea and normal AL, a significant positive correlation shows up between AL and IOP, although, again, these eyes were not glaucomatous. This is in contrast to the report by Lee et al,[20] who found no correlation between IOP and AL. Whether the growth of eyes with small corneas is under the influence of the same factors as eyes with normal corneas thus remains to be investigated.

In this study, it is of note that the age was significantly different between the 2 subgroups when stratified according to AL: older children had longer eyes. This is in agreement with the documented growth of the eye in the initial years of life and suggests, as already mentioned, that the pathology resulting in a small cornea does not hinder normal growth of the eye, although this could not be confirmed by this study, given that the study patients were not followed longitudinally for changes in the AL.

Equally interesting in this study is the significant correlation between the CCT and the AL in each of the 2 subgroups on stratification of the study eyes into short and normal AL subgroups. This raises the same previous question about the factors controlling eye growth and development in eyes with small corneas.

Furthermore, stratification of the study according to AL did not change any of the correlations observed between CCT and other study parameters, emphasizing the fact that it is the CCT, rather than the AL, that dictates the biomechanical behavior of the cornea toward the applanation forces of the tonometer. Hence, the CCT is to be taken into consideration for the interpretation of the IOP measurements in eyes with microcornea, irrespective of the AL.

The etiology of increased CCT after cataract surgery in children has been ascribed to a number of causes, including endothelial cell injury by the mechanical stress of cataract surgery,[21] and interruption of normal corneal development and thinning.[22] The fact that eyes with smaller corneal diameters had thicker corneas after congenital cataract surgery than eyes with normal corneal diameters after congenital cataract surgery may favor a developmental anomaly of the cornea as a cause.

TABLE 4. Clinical Examination Data for Short and Normal Axial Length (AL) Eyes

	Mean ± SD (Range)	
	Patients With AL < 21.0 mm	Patients With AL > 21.0 mm
Central corneal thickness (μm)	676.44 ± 69.28 (564-822)	652.08 ± 77.41 (545-944)
Corneal diameter (mm)	8.8 ± 1.0 (7.0-10.0)	9.1 ± 0.4 (8.5-10.0)
Measured intraocular pressure (mm Hg)	10.6 ± 5.0 (3-23)	11.4 ± 6.7 (6-32)
Cup/disc ratio	0.1 ± 0.2 (0-0.5)	0.1 ± 0.1 (0-0.4)
Axial length (mm)	18.48 ± 1.80 (14.56-20.95)	23.31 ± 1.47 (21.34-25.98)

This study has limitations. Although the controls were properly demographically matched with the study eyes, yet, it would have been more informative to use aphakic, rather than phakic, children with a normal corneal diameter. Nevertheless, aphakic eyes after congenital cataract surgery may as well be associated with other congenital ocular anomalies that can act as confounders. Hence, the authors chose not to use these eyes as controls. Our records do not include data on the cataract morphology in the study eyes; this may have affected the CCT and may have been associated with other corneal biomechanical abnormalities. Finally, control eyes lacked AL data. However, there is a paucity of the literature addressing this issue of CCT in eyes with microcornea-microphthalmia, and, to the best of the authors' knowledge, this study is the first report on this issue in children in this part of the world, the Middle East, an area of the world that is heavily populated, and where consanguineous marriages, with their implications on the offspring's health, are particularly common. Although the study was conducted on Egyptians exclusively, who are mostly whites, information on ethnicity in this study is to be inferred only, and is not explicit, as the information about ethnicity is not routinely recorded in patients' charts.

In conclusion, aphakic eyes with microcornea, with or without a short AL, have a thicker than normal CCT and have a greater than normal measured IOP, despite the absence of glaucoma. The measurement of CCT is recommended in the assessment of aphakic eyes for possible glaucoma. The measured IOP, although a reliable parameter, in isolation does not provide a diagnosis of glaucoma and must be viewed in conjunction with other patient findings, such as the cup/disc ratio, the progression of which over time must be considered for a more solid diagnosis.

REFERENCES

1. Kenyon KR, Starck T, Cockerham G, et al. Corneal dysgeneses, dystrophies, and degenerations. In: Albert D, Miller J, Azar D, Blodi B, eds. *Albert & Jakobiec's Principles and Practice of Ophthalmology*, 3rd ed. Philadelphia, PA: W.B. Saunders; 2008:498.
2. Salmon JF, Wallis CE, Murray AD. Variable expressivity of autosomal dominant microcornea with cataract. *Arch Ophthalmol*. 1988;106:505–510.
3. Wang KJ, Wang S, Cao NQ, et al. A novel mutation in CRYBB1 associated with congenital cataract-microcornea syndrome: the p. Ser129Arg mutation destabilizes the betaB1/betaA3-crystallin heteromer but not the betaB1-crystallin homomer. *Hum Mutat*. 2011;32:E2050–E2060.
4. Khan K, Al-Maskari A, McKibbin M, et al. Genetic heterogeneity for recessively inherited congenital cataract microcornea with corneal opacity. *Invest Ophthalmol Vis Sci*. 2011;52:4294–4299.
5. Lim Z, Muir KW, Duncan L, et al. Acquired central corneal thickness increase following removal of childhood cataracts. *Am J Ophthalmol*. 2011;151:434–441.
6. Keech RV, Tongue AC, Scott WE. Complications after surgery for congenital and infantile cataracts. *Am J Ophthalmol*. 1989;108:136 –141.
7. Mills MD, Robb RM. Glaucoma following childhood cataract surgery. *J Pediatr Ophthalmol Strabismus*. 1994;31:355–360.
8. Muir KW, Jin J, Freedman SF. Central corneal thickness and its relationship to intraocular pressure in children. *Ophthalmology*. 2004;111:2220 –2223.
9. Hussein MA, Paysse EA, Bell NP, et al. Corneal thickness in children. *Am J Ophthalmol*. 2004;138:744 –748.
10. Dai E, Gunderson CA. Pediatric central corneal thickness variation among major ethnic populations. *J AAPOS*. 2006;10:22–25.
11. Raab EL, Aaby AA, Bloom JN, et al. Diseases of the cornea and anterior segment. In: *Pediatric Ophthalmology and Strabismus*: Basic and clinical science course by the American Academy of Ophthalmology; 2012:212.
12. Gal A, Rau I, El Matri L, et al. Autosomal-recessive posterior microphthalmos is caused by mutations in PRSS56, a gene encoding a trypsin-like serine protease. *Am J Hum Genet*. 2011;88:382–390.
13. Filous A, Osmera J, Hlozanek M, et al. Central corneal thickness in microphthalmic eyes with or without history of congenital cataract surgery. *Eur J Ophthalmol*. 2011;21:374–378.
14. Simon JW, O'Malley MR, Gandham SB, et al. Central corneal thickness and glaucoma in aphakic and pseudophakic children. *J AAPOS*. 2005;9:326–329.
15. Egbert JE, Wright MM, Dahlhauser KF, et al. A prospective study of ocular hypertension and glaucoma after pediatric cataract surgery. *Ophthalmology*. 1995;102:1098–1101.
16. Muir KW, Duncan L, Enyedi LB, et al. Central corneal thickness: congenital cataracts and aphakia. *Am J Ophthalmol*. 2007;144:502–506.
17. Nilforushan N, Falavarjani KG, Razeghinejad MR, et al. Cataract surgery for congenital cataract: endothelial cell characteristics, corneal thickness, and impact on intraocular pressure. *J AAPOS*. 2007;11:159–161.
18. Jaafar MS, Kazi GA. Normal intraocular pressure in children: a comparative study of the Perkins applanation tonometer and the pneumotonometer. *J Pediatr Ophthalmol Strabismus*. 1993;30:284–287.
19. Tai TTT, Mills MD, Beck AD, et al. Central corneal thickness and corneal diameter in patients with childhood glaucoma. *J Glaucoma*. 2006;15:524–528.
20. Lee AJ, Saw SM, Gazzard G, et al. Intraocular pressure associations with refractive error and axial length in children. *Br J Ophthalmol*. 2004;88:5–7.
21. Amino K, Miyahara S, Tanihara H. Corneal thickness in eyes following pars plana lensectomy for congenital cataract. *Jpn J Ophthalmol*. 2004;48:169–171.
22. Griener ED, Dahan E, Lambert SR. Effect of age at time of cataract surgery on subsequent axial length growth in infant eyes. *J Cataract Refract Surg*. 1999;25:1209–1213.