Med & Health Dec 2020; 15(2): 66-84 https://doi.org/10.17576/MH.2020.1502.09

ORIGINAL ARTICLE

Evaluation of the Relationship between Corneal Diameter and Lens Diameter in Children

WONG CL[1,2], BASTION MLC[1], ROPILAH AR[1], JAMALIA R[2]

[1]Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia
[2]Department of Ophthalmology, Hospital Kuala Lumpur, Ministry of Health Malaysia, Kuala Lumpur, Malaysia

ABSTRAK

Kajian ini bertujuan untuk mengkaji hubung kait antara diameter kornea dan diameter kanta di kalangan kanak-kanak. Kajian ini melibatkan sejumlah empat puluh kanak-kanak (40 mata) yang kurang daripada 4 tahun yang menjalani pemeriksaan, prosedur atau pembedahan di Hospital Kuala Lumpur dari Januari 2010 sehingga September 2011. Pemeriksaan dijalankan dengan menggunakan bius am di dewan bedah. Diameter kornea diukur dengan 'Holladay-Godwin cornea gauge' sementara diameter kanta diukur dengan menggunakan mesin ultrasound yang mempunyai resolusi tinggi 'ultrasound biomicroscope (UBM)'. Purata umur populasi kajian adalah 24.7 ± 12.1 bulan. Purata diameter kornea melintang adalah 11.62 ± 0.50 mm, lebih besar berbanding dengan purata diameter kornea menegak yang berukuran 11.20 ± 0.58 mm. Purata diameter kanta adalah 7.94 ± 0.47 mm. Diameter kornea didapati mempunyai korelasi positif yang sederhana dengan diameter kanta (r=0.479, p=0.002). Terdapat hubung kait yang kukuh di antara diameter kanta dengan umur pesakit (r=0.718, p<0.001). Diameter kanta boleh dikira dengan menggunakan formula: [Diameter kanta (mm) = 7.010 + 0.021 Diameter kornea (mm) + 0.028 Umur (bulan)] (r^2=0.52). Kesimpulannya, terdapat hubungkait positif yang sederhana di antara diameter kornea dengan diameter kanta. Mesin UBM boleh digunakan untuk mengukur bag kanta mata secara langsung sebelum pembedahan.

Kata kunci: diameter kanta, diameter kornea, kanak-kanak, pengukur kornea, ultrasound bio microscopy

Address for correspondence and reprint requests: Mae-Lynn Catherine Bastion. Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-91455983 Email: maelynnb2003@yahoo.com

ABSTRACT

Primary intraocular lens (IOL) implantation has gained acceptance for management of infantile cataracts because of the advantage of reduced amblyopia risk. The aim of the study was to investigate the association between corneal diameter as measured from the white-to-white distance and natural lens diameter in children. This association may aid intraocular lens selection following cataract removal in infants and young children. A cross-sectional study was performed on forty eyes from 40 children less than 4 years, who needed to be examined, were planned for a procedure or operation under general anaesthesia. Subjects were recruited from Eye Clinic,Kuala Lumpur General Hospital from January 2010 to September 2011. Corneal diameter was measured with Holladay-Godwin corneal gauge while lens diameter was measured with ultrasound biomicroscope (UBM) during surgery. For the results, mean age of subjects was 24.7 $\pm$ 12.1 months. Mean corneal diameter was 11.62 $\pm$ 0.50 mm horizontally and 11.20 $\pm$ 0.58 mm vertically. Mean horizontal lens diameter was 7.94 $\pm$ 0.47 mm. A medium positive correlation was found between mean horizontal corneal diameter and lens diameter (r=0.479, p=0.002). Lens diameter had a strong correlation with patient's age (r=0.718, p<0.001). Lens diameter can be calculated by using this model of equation: [Lens diameter (mm) = 7.010 + 0.021 Corneal Diameter (mm) + 0.028 Age (months)] (r^2=0.52). In conclusion, there was a moderate positive correlation between corneal and lens diameter. UBM can be used to measure lens capsular bag size directly preoperatively.

Keywords: children, corneal diameter, corneal gauge, lens diameter, ultrasound bio microscopy

INTRODUCTION

Primary intraocular lens (IOL) implantation has now gained acceptance for the management of infantile cataracts because of the advantages it offers to reduce the risk of amblyopia. A critical issue about IOL implantation in children is that the paediatric eye is smaller than the adult eye. This is especially the case up to the age of 3 years. Therefore, the implantation of IOLs, which are adult-sized, would understandably not be appropriate. Currently available adult-sized IOLs are slightly oversized in relation to capsular bag measurements in infants and young children and possibly do not fit into tiny eyes. The possible sequelae of implantation of adult-sized IOLs into the smaller, by comparison, capsular bag of young children include decentration of the IOL, and marked capsular bag stretching, resulting in capsular folds and striations and stress on the zonular processes. The capsular folds promote migration of lens epithelial cells toward the visual axis, leading to posterior capsular opacification and capsular phimosis (Wilson et al. 2005).

It has been recommended by the IOLunder2 study in the United Kingdom that IOLs not be placed in children under the age of two years due to a higher risk of complications including reoperation in these extremely young individuals for posterior capsular opacification and because lens implantation did not reduce the risk of glaucoma (Solebo et al. 2018). The group has recommended that contact lenses be the preferred option for correction of aphakia for those under two years of age. However, IOL is recommended for those aged two years and above.

On the other hand, results of a meta-analysis conducted by the American Academy of Ophthalmology recommended that the age for IOL implantation be at six months of age. The study of 13 published articles on this subject provides convincing evidence to suggest that implantation of an IOL is safe with reasonably minimal side effects in children above six months of age (Lambert et al. 2019). In these young children, it is the size of the lens capsular bag that limits in-the-bag implantation (Wilson et al. 1994; Bluestein et al. 1996; Dong & Joo 2001). Therefore, knowing the capsular bag size at the time of implantation surgery may be helpful in selecting the most appropriate design and model of intraocular lens for these vulnerable, young eyes.

To date, there is no perfect system to determine the internal lens or capsular bag diameter. Traditional teaching was that measurement of the corneal diameter or white-to-white diameter (WTW) allowed the dimensions of intraocular structures and spaces to be measured indirectly. However, this evaluation is only an approximation and depends on the estimation of the WTW distance externally.

Several studies have been conducted to elucidate the association between WTW corneal diameter with internal ocular dimensions. Some studies on this used cadaver eyes (Wilson et al. 1994; Bluestein et al. 1996; Dong & Joo 2001; Khng & Osher 2008). Conversely, various imaging techniques have been used in vivo to measure internal ocular dimensions. For instance, ultrasound biomicroscopy (UBM), (Kim et al. 2008; Oh et al. 2007; Pop et al. 2001) magnetic resonance imaging (MRI), (Fea et al. 2005; Strenk et al. 1999) optical coherence tomography (OCT), (Kohnen et al. 2006; Radhakrishnan 2005) scanning slit photography and rotating Scheimpflug photography (Jain et al. 2006) have been described. The results of these studies were conflicting with significant results in some studies, but not others. In a study by Jain et al., a regression formula was found that was able to utilise biometric parameters to determine the diameter of the empty capsular bag in vivo. The formula used the independent factors, keratometric power and axial length (Jain et al. 2006; Radhakrishnan 2005; Vass et al. 1999).

A recent study by Khng & Osher in 2008 tested the relationship between horizontal and vertical corneal diameter and lens diameter using 76 human cadaver eyes. One of the authors (R.H.O) with 27 years' experience measuring WTW horizontal corneal diameter of each surgical patient, observed that WTW corneal diameter gave information that was useful on capsular bag diameter. However, this study reported that the relationship between corneal and lens diameter was not a strong one (r=0.32). They concluded that the dimensions of the human crystalline lens could not be predicted when callipers were used to measure the WTW distance.

Not much has been reported regarding paediatric crystalline lens measurement and the appropriate size of paediatric IOLs according to the patient's age. To predict the lens size in a paediatric patient, (Bluestein et al. 1996) 50 fresh, autopsied eyes from patients ranging in age from 1 day to 16 years were examined. The following readings were calculated: anterior-posterior, vertical, and horizontal lengths of the eyeball and the corneal, lens and zonular free zone diameters. It was found that both age and corneal diameter could predict crystalline lens size (r=0.72, r=0.71). A growth curve was developed for the equatorial lens diameter that aided in the selection of IOL designs for tiny eyes. This growth curve was likewise able to illustrate that during the period of birth to 2 years of age, the globe, lens and capsular bag underwent its most rapid period of growth.

Interestingly, there are also racial differences in the dimensions of the cornea and lens in infants and young children. For instance, a study of infants born in a Nigerian hospital in 1993 found the mean corneal diameter to be 10.26 mm (SD±0.59 mm) which was significantly higher than that reported for Caucasian infants at that time. The study also observed an increase in cornea diameter over time until the age of 34 weeks (Ashaye & Olowu 2006). Mashige in 2013 reported that cornea diameter seemed to increase until the age of 10-20 and then there was a decline in size in the elderly. The study also noted differences in the dimensions of Asian and Caucasian eyes postulated to be due to the differences in height. There was, therefore, a need to characterise the dimensions of the eyes of young children from a South-East Asian heritage.

The current practice of measuring WTW cornea diameter to decide on IOL implantation in children is still controversial. In the past, no method was capable of measuring the lens size in vivo preoperatively. Most of the previous studies were conducted using cadaver eyes.

UBM is a new method to measure internal ocular dimension in vivo. UBM was introduced by Pavlin et al. (1992), enabling high magnification and two-dimensional images of the anterior portion of the eye at high resolution in a living person. While the UBM unit has been used to measure sulcus diameter directly, there are very few formal clinical studies using high-frequency UBM to measure lens capsular bag diameter in vivo, especially in children (Rondeau et al. 2004; Kawamorita et al. 2010; Kim et al. 2008; Oh et al. 2007; Pop et al. 2001). A study by Zare et al. (2011) reported the application of UBM in a case of anterior megalophthalmos with cataract, planned for surgery. The UBM examination found a normal diameter of the capsular bag despite ciliary ring enlargement. They had suggested that in cases of anterior megalophthalmos where there is no phacodonesis, the actual size of the capsular bag can be measured by UBM. This would then reduce the need for a custom IOL to be designed. Modesti et al. also published a study regarding the use of 35 MHz UBM in adults, whereby the preoperative and postoperative size and lens capsular bag movements could be analysed (Modesti et al. 2011).

Since there is little data available on the crystalline lens dimension in children, especially in very young children and the controversy of using the WTW to estimate the internal ocular structure dimension, this study aimed to evaluate the relationship between corneal and crystalline lens diameter in children under the age of 4 years. Specifically, the study seeks to measure the corneal diameter with corneal gauge and lens width using UBM in children under the age of 4 years and to correlate the corneal diameter with the lens diameter; correlate the corneal and lens diameter with age and to determine a regression formula based on corneal diameter and age which helps predict the lens capsular bag diameter.

MATERIALS AND METHODS

This cross-sectional study was performed from 1st January 2010 to 30 November 2011 at the Department of Ophthalmology of Hospital Kuala Lumpur, a busy service hospital in Kuala Lumpur, the capital city of Malaysia. Ethics approval from Research and Ethics Committee, Faculty of Medicine, University Kebangsaan Malaysia (UKM) and National Medical Research Register (NMRR) of the Ministry of Health Malaysia were obtained before commencement of the study. The research also adhered to Malaysian Good Clinical Practice (MGCP) 2nd edition January 2004 guidelines and was conducted following the principles of the Declaration of Helsinki.

Inclusion criteria for the study were term children between 1 day to 4 years of age, children with at least one normal eye, fit to undergo examination, procedure or operation under general anaesthesia and children who were stable enough for ocular examination during anaesthesia. Children were excluded from the study if they had gross ocular abnormality or pathology in both eyes, last known ocular injury, previous ocular surgery on the eye to be studied, intrauterine growth retardation (IUGR), prematurity, syndromic baby, eye found to have pathology during examintaion under anaesthesia (EUA), parent's refusal to have their children to be included or chemotherapy.

All children aged from 1 day to 4 years who were admitted for EUA, procedure or operation and fulfilled the inclusion criteria were enrolled in the study. The review of the patients was conducted at the Eye Operation Theatre of the hospital. The ethical approval was obtained from two Institutional Ethics Committee. The first approval was from the Universiti

Kebangsaan Malaysia Medical Centre Research and Ethics Committee (FF-062-2011). The other approval was granted by the Ministry of Health Malaysia through its Clinical Research Centre (NMRR-09-974-4858). Based on Graybill (1961), Guenther (1977) and Zar (1999), a sampled size of 31 eyes achieves a 90% power to detect a difference of 0.20 between the null hypothesis correlation of 0.90 and the alternative hypothesis correlation of 0.70 using a two-sided hypothesis test with a significance level of 0.05. This sample size can be calculated using the power and sample size calculation programme PASS 2008, version 08.0.5, copyright by Dr Jerry L. Hintze, Kaysville, Utah, USA. Hence, 40 patients were recruited to account for drop-out.

Diameter in this study was defined as the length of a straight line passing through the centre of the cornea and connecting opposite points on its circumference. In this case, the corneal diameter was defined as the corneal WTW measurement along its horizontal and vertical meridian. The measurement was done by using Holladay-Godwin corneal gauge with 0.5mm increments. Cornea gauge which was first introduced by Kiskis et al. (1985), is a series of plastic plates with holes of different diameters in quarter-millimetre increments. The cornea gauge (Asico, USA) used in this study consisted of a double-sided hexagonal plate with semi-circles ranging from 9.0-14.0 mm in 0.5 mm increments representing the semi-circle diameter printed on the margin. This device was held at arm's length from the examiner and approximately 1.0 mm away from the cornea. The diameter of the half circles was comparable to the WTW corneal diameter.

Crystalline lens diameter was defined as the length of a straight line passing through the centre of the lens and connecting opposite points on its circumference. The measurement was performed using the 50MHz UBM. Empty lens capsular bag diameter was defined as the crystalline lens diameter [mm] + 1.0 mm (Bluestein et al. 1996; Khng & Osher 2008; Puvanachandra & Lyons 2009; Richburg & Sun 1983; Wilson et al. 1994). This is due to the increase in capsular bag dimension by 1.0 mm after the lens material has been removed either manually or via phacoemulsification. A normal eye was defined as one in which there was an absence of structural abnormality in the anterior and posterior segment of the eye on EUA with visual function appropriate for age. A full-term baby was one that was born between 38 to 42 weeks of gestation.

Children who fulfilled the selection criteria for the study were identified. The purpose, nature of the study and the examinations required were explained to the parents or guardians. Those who agreed to participate had to sign the informed consent form at study entry. Demographic data, past medical history and past ocular history were obtained from patients' notes and parents. All data in this study was kept confidential.

Examination of the patients was done under general anaesthesia in the Ophthalmology operation theatre. The patient's pupil was dilated for

Figure 1: Crystalline lens and anterior segment axial cross-section as captured by the Quantel Aviso UBM 50Mhz probe

examination purpose with guttae tropicamide, guttae phenylephrine or subconjunctival mydracaine. A speculum was used to open the eyelid. The WTW corneal diameter on the selected eye was measured using Holladay-Godwin cornea gauge. Three measurements were taken for both horizontal and vertical WTW corneal diameter. Mean of three readings was used.

UBM examination was done by the same examiner (investigator W.C.L) using Aviso Quantel Medical, Cournon d'Auvergne, France with a 50 MHz transducer probe. The probe was prepared by instilling distilled water into the transducer which was sealed tight with a disposable single use membrane. Lubricant gel was used as the contact media. The probe was placed at the centre and horizontally. Images were captured in motion video over the centre of the pupil. At least three standard axial images sections in video clips were obtained and saved in AVISO UBM software programme, Cournon d'Auvergne, France.

Measurement of the lens diameter from the video clips was done in a separate setting. The maximum pupil diameter from images captured allowed the horizontal cross-section to be found. The best quality frames that were most illustrative were chosen from each video clip. The lens diameter was measured using the calliper incorporated in AVISO UBM software. The lens diameter was measured from one end to another end of the anterior capsule at the equator (Figure 1). Mean of the best three readings from video clips was used. To reduce the risk of infection to the children, the speculum and cornea gauge were sterilized with a disinfectant agent, and a single-use disposable membrane (Sonar Aid, Geistlic Pharma, Wolhusen, Switzerland) for UBM was used.

Data were analysed using Statistical Package for Social Science (SPSS) version 16.0 (IBM, Armonk, New York, USA). Kolmogorov-Smirnov test was used to determine normality of the distribution of each group. Each group was found to have a mean almost equal to the median, skewness between -2.0 and +2.0 and bell-shape distribution.

Table 1: Demographic characteristic of the study population

Characteristics		Number (n)
Age (months)	Mean	24.7 (12.1)
	Minimum	4.2
	Maximum	46.0
Gender	Male	22
	Female	18
Ethnicity	Malay	27
	Chinese	4
	Indian	5
	Others	4
Eyes	Left	18
	Right	22
Age of children (months)	0-6	2
	6-12	6
	12-18	2
	18-24	9
	24-30	7
	30-36	4
	36-42	4
	42-48	6

Consequently, the data were normally distributed. Pearson correlation coefficient could be used to investigate at the relationship between corneal diameter, lens diameter and age. The independent t-test was performed to compare corneal diameter and lens diameter between gender. Prediction value of lens diameter was measured using bivariate linear regression. The dependent variable was the horizontal lens diameter. The independent variable was horizontal WTW corneal diameter and age. Statistical significance was presumed to occur at the p-value less or equal to 0.05.

RESULTS

From January 2010 to September 2011, 40 patients (40 eyes) who fulfilled the study inclusion criteria were included in the study. Mean age of the study population was 24.7±12.1 months. The youngest patient was 4.2 months, and the oldest patient was 46 months old. There were nine patients less than one year old, 12 patients were between one to two years old, 12 patients were between two to three years old, and seven patients were between three to four years old. Table 1 shows the distribution of ages of the 40 subjects involved in this study. Table 1 also summarises the demographic characteristic of the study population. The number of males was slightly more than females. Among the subjects,

Table 2: Distribution of study population by reasons for anesthesia

Reasons for anaesthesia		Number of patients
1	EUA for unilateral retinoblastoma	11
2	Prosthesis / contact lens fitting	4
3	Lens aspiration and intraocular lens implantation	3
4	EUA for pseudophakic / aphakic	3
5	EUA post anterior segment trauma (eg. Post corneal T&S, hyphema)	3
6	Enucleation	2
7	EUA for unilateral congenital glaucoma / anterior segment dysgenesis	2
8	Intralesional steroid for lid capillary hemangioma	2
9	EUA+ fundus fluorescein angiography + laser for Coat's disease	2
10	EUA for persistent fetal vasculature	1
11	Squint surgery	1
12	EUA for leukocoria	1
13	Dermoid excision	1
14	Incision and drainage for lid abscess	1
15	Trans pars plana vitrectomy + endoprocedure for vitreous haemorrhage	1
16	Orbital hemangioma/ teratoma	1
17	EUA + UBM TRO medulloepithelioma	1
	Total	40

there were 27 Malays, 5 Indians, 4 Chinese, and 4 from other ethnic groups as recorded in the national register of the father which included 1 Orang Asli, 1 Punjabi, 1 Iban and 1 Indonesian (Table 1). Table 2 shows the distribution of the study population by reasons for a patient to undergo general anaesthesia. Out of the 40 patients, 11 patients (27.5%) were admitted for EUA for retinoblastoma. All these patients had not undergone chemotherapy at the time of examination. Two patients were excluded from the study after they were found to have an abnormality in the eye being examined. One of them was found to have congenital glaucoma, and the other had retinoblastoma. There was no complication encountered during

Table 3: Measurement of corneal and lens diameter

	Horizontal WTW Corneal Diameter (mm)	Vertical WTW Corneal Diameter (mm)	Horizontal Lens Diameter (mm)
Mean ± SD	11.62 ± 0.54	11.20 ± 0.58	7.94 ± 0.47
Minimum	10.50	10.00	6.86
Maximum	12.50	12.33	8.70

Table 4: Corneal and lens diameter according to age group

Age (months)	Mean (mm) ± SD			
	≤12 n=9	**12< to ≤24 n=12**	**<24 to ≤36 n=12**	**<36 to ≤48 n=7**
Horizontal WTW corneal diameter	11.09 ± 0.48	11.68 ± 0.36	11.74 ± 0.48	11.98 ± 0.30
Lens diameter	7.37 ± 0.34	7.87 ± 0.37	8.20 ± 0.33	8.34 ± 0.20

the study.

The mean horizontal corneal diameter of the study population was 11.62 mm ±0.50 (Table 3). The smallest horizontal corneal diameter was 10.50 mm, belonging to two patients aged 4.2 months old and 5.5 months old. The largest horizontal corneal diameter was 12.5 mm belonging to two patients aged 35 months and 43.5 months. When divided into sub-age group, the mean corneal diameter was 11.09±0.48 mm for children at the first year of life, 11.68±0.36 mm at 1-2 years, 11.74±0.48 mm at 2-3 years and 11.98±0.30 mm at 3-4 years (Table 4).

There was a disparity in the horizontal and vertical diameters of the cornea where the mean vertical corneal diameter was smaller than mean horizontal corneal diameter. The mean vertical corneal diameter of the study population was 11.20±0.58 mm. The smallest vertical corneal diameter was 10.0 mm belonging to patients aged 4.2 months, 5.5 months and 23 months. In contrast, the largest vertical corneal diameter was 12.33 mm belonging to a patient who was 43.5 months old. The mean female horizontal corneal diameter was slightly larger than male but not statistically significant (p= 0.33).

The mean horizontal lens diameter of the study population measured by 50MHz UBM was 7.94±0.47 mm (Table 3). The smallest was 6.86 mm, which belonged to a patient aged seven months. On the other hand, the largest horizontal lens diameter was 8.70 mm belonging to a patient who was 35 months old. When divided into

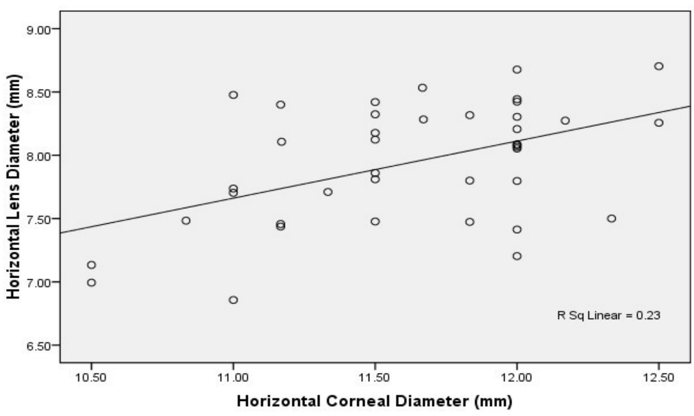

Figure 2: Correlation between corneal diameter and lens diameter

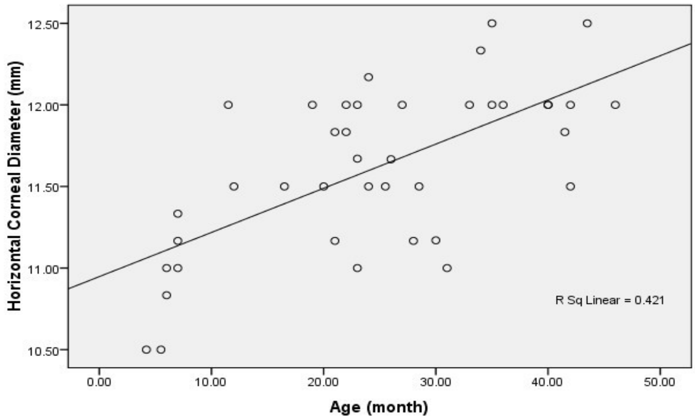

Figure 3: Correlation between corneal diameter and age

sub-age groups, the mean lens diameter was 7.37±0.34 mm for children at the first year of life, 7.87±0.37 mm at 1-2 years, 8.20±0.33 mm at 2-3 years and 8.34±0.20 mm at 3-4 years (Table 4).

The horizontal corneal diameter of the study population correlated positively with their horizontal lens diameter. The correlation was moderate (r=0.479). There was an increment of horizontal corneal diameter with increasing horizontal lens diameter. This relationship was statistically significant (p=0.002, <0.05) (Figure 2). The horizontal corneal diameter of the study population also correlated positively with their age (r=0.649). In particular, the horizontal cornea diameter increased with age. This relationship was statistically significant (p<0.001) (Figure 3). The horizontal lens diameter of the study population had a strong positive correlation with their age (r=0.718). The horizontal corneal diameter increased with increasing age. This relationship was statistically significant (p<0.001) (Figure 4).

Linear regression test was used to produce a formula to predict the horizontal lens diameter in this study

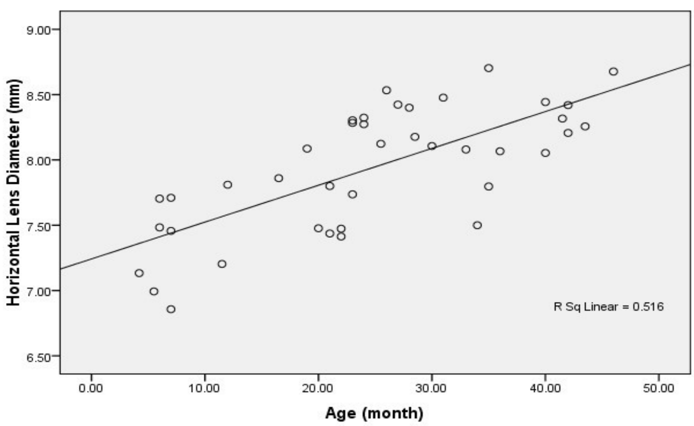

Figure 4: Correlation between lens diameter and age

population by using their horizontal corneal diameter and age. Based on the results of this study, the lens diameter of the study population can be calculated using this model of the equation:

Lens diameter [mm] = 7.010 + 0.021 Corneal diameter [mm] + 0.028 Age [months]

Age and corneal diameter explained a significant proportion of variance in lens diameter, R^2=0.516 F(2,40)=19.719, p<0.001. This equation can predict 52% of the factors that affect the lens diameter.

DISCUSSION

Few studies have been done to evaluate the relationship between corneal diameter and lens diameter, especially in children younger than four years of age, and this was the first study in Malaysia looking into this issue. To date, the majority of studies about corneal diameter and lens diameter have been conducted in Caucasian, Middle Eastern or African eyes. In this study, by measuring corneal and lens diameter, we obtained valuable data on corneal and lens diameter in the eyes of South-East Asian children.

Advances of imaging technology have introduced alternative methods of measuring the intraocular structures and spaces in vivo. In this study, we used Holladay-Godwin corneal gauge to measure external WTW corneal diameter and 50MHz UBM to measure lens diameter in vivo. It was a challenging task to recruit young children as study subjects for research because they were usually not easily examined in the clinic. Therefore, we chose those children who needed to be examined, who were planned for a procedure or operation under general anaesthesia and took the opportunity to examine the fellow eye with no known ocular abnormalities. The majority of the patients in this study were admitted for examination under anaesthesia for retinoblastoma since our centre is the paediatric ophthalmology centre of the Ministry of Health Malaysia. We excluded those patients already started or completed chemotherapy as we believe chemotherapy might affect the child's wellbeing and may have an effect in the normal healthy growth of the child and eye (Olshan et al. 1992).

The results of this study indicate that the mean corneal diameter measured by corneal gauge was 11.62±0.50 mm [range from 10.5-12.5 mm] and the mean vertical WTW was 11.20±0.58 mm [range from 10.00 to 12.33 mm], somewhat lower than the horizontal corneal diameter. These dimensions were slightly smaller when compared to the study by (Khng & Osher 2008; Puvanachandra & Lyons 2009) in which the mean corneal diameter measured with callipers was reported as 11.86±0.99 mm and with photographic measurements was 11.91±0.94 mm in patients of an average age of 3.5 years. However, our mean corneal diameter was larger when compared to a study by (Müller & Doughty 2002) who reported the mean corneal diameter measured by millimetre rule and close up photograph was 11.48 mm for children with a mean age of 10.1 years. We believe that the differences of our study result on the corneal diameter compared to others could be due to differences in the composition of the populations measured, method of measuring and the age of the study population. In particular, Holladay-Godwin corneal gauge was used for measurement of corneal diameter, which is not a precise method. However, this was the most accurate instrument available to us at the time. Our result also showed a strong positive correlation between corneal diameter and age.

The measurement of the internal lens dimension is more difficult and complicated when compared to measuring external corneal diameter. Most of the previous studies in this aspect used cadaveric eyes. With advances in imaging technology, we used the 50 MHz UBM in this study to measure lens diameter in vivo. Mean horizontal crystalline lens diameter of the study population was 7.94±0.47 mm ranging from 6.86-8.70 mm. It would have been useful to correlate corneal and lens diameter with lens thickness and axial length to consider the overall size of the paediatric eye. However, this was not an objective of this study and should be investigated further.

Looking at the study results by Bluestein et al. (1996), they reported mean lens diameter of cadaveric eyes were 6.0 mm at birth, 6.8 mm at two months, 7.1 mm at three months, 7.6 mm at six months to nine months, 8.4 mm at 21 months, 8.5 mm at two to five years, and 9.3 mm at age 16 years. Our local data in Table 4 shows slightly smaller lens diameter according to the different age groups. This could be due to geographical factors and different ethnicity. The other differences that may be taken into account are the instruments used to measure the lens diameter. Furthermore, the post-mortem changes and fixation on the results is unknown because cadaveric eyes may be susceptible to the inevitable distortions of the preparation process. From this study, we can conclude that the crystalline lens diameter in our local children population is slightly smaller compared to Caucasian eyes. Our study demonstrated a significant strong relationship between lens diameter and age, r=0.718, which is consistent with the result by Bluestein et al. (1996) which reported r=0.72.

Published studies reported mean adult lens diameter ranging from 9.28 mm to 9.6 mm (Dong & Joo 2001; Fea et al. 2005; Khng & Osher 2008; Wilson et al. 2005) which alerted us that in very young children especially in children less than one year old, the lens diameter has not reached adult size. Yet, adult size IOLs are implanted into these children's eyes. Caution should be taken to look for any complications of IOL implantation since there might not be enough space for adult size IOL implantation in small children eyes. When patients reach around 2-4 years of age, they have almost achieved adult size lenses. It is reasonable to implant adult size IOLs in this group of patients.

When comparing the lens diameter between genders, although our results showed that the lens diameter in females was slightly larger than males, this, can be due to differences in the mean age of both groups because the male cohort (21.80±12.16 months) was a bit younger than the female (28.28±11.30 months). However, the mean values of males and females were not significantly different. We did not make a comparison between ethnicity because the distribution of ethnics was not uniform, hence may not be comparable. We were unable to get an equal distribution of subjects from each ethnic group due to limited study time.

The main aim of our study was to investigate the association between corneal diameter and lens diameter. Our research hypothesis was corneal diameter in children was positively correlated with lens diameter. Although there were a few studies published recently which reported the use of UBM to measure the lens capsular bag directly, to date, there is no published literature reporting the use of UBM to measure lens capsular bag diameter in children and correlating it with the external corneal diameter (Modesti et al. 2011; Zare et al. 2011). This is an essential issue since it has been a practice in pediatric cataract surgery to decide whether to implant IOLs based on external WTW corneal diameter.

Our results showed that the horizontal corneal diameter of children less than four years old has a modest positive correlation with their horizontal lens diameter, r=0.479, p=0.002. Our results are close to the results of the study done by (Khng & Osher 2008) who reported a weak association between the measurement of the cornea and lens diameter (r=0.32). The authors observed that it was impossible for the dimensions of the human crystalline lens to be predicted using WTW corneal diameter.

Our results are modest compared to earliest studies (Bluestein et al. 1996; Dong & Joo 2001) which showed a strong relationship between corneal diameter and lens diameter. Both studies showed a Pearson coefficient, r of 0.71. According to Bluestein et al. (1996), age and corneal diameter were both able to predict the crystalline lens size (r=0.72, r=0.71, respectively). Anterior-posterior axial length (r=0.77) was found to be the best parameter capable of estimating the crystalline lens size and therefore, the size of the capsular bag. A multiple linear regression analysis which incorporates all these factors is: Crystalline lens = 1.4 + 0.22 (age) + 0.18 (anterior-posterior axial length of the globe) + 0.20 (cornea with a coefficient of determination of R^2=0.69.

Dong & Joo in 2001 using 62 postmortem eyes from 38 adult patients with no significant ocular pathology, measured cornea and lens diameter using an operating microscope with a video monitor and an appropriate scale. These two sets of measurements were then evaluated. They found that there is a significant relationship between corneal diameter and lens diameter (correlation coefficient=0.711, p<0.001). There was also a significant correlation between corneal diameter and axial length (correlation coefficient=0.788, p<0.001). From these two studies, axial length and corneal diameter can give surgeons a helpful clue to the expected capsular bag size and is a crucial parameter for selecting the correct IOL size (Bluestein et al. 1996; Dong & Joo 2001).

Our results seem to indicate individual specificity in corneal diameter and lens diameter. The potential error in estimating lens diameter by using WTW corneal diameter comes from the variability in the difference between WTW and lens diameter since they do not have a strong correlation. Therefore, it may not be reliable just to estimate lens diameter based on the external WTW corneal diameter. Lens diameter determined by UBM would be better than the conventional method of predicting it based on outer WTW corneal diameter to decide on IOL implantation.

Currently, although there is no absolute contraindication for primary implantation in infants, a corneal diameter less than 9.0 mm is a relative contraindication (Wilson et al. 2005). It is postulated that the anterior chamber in a small eye may lack sufficient space to safely ensure that corneal endothelial touch will not occur during or after implantation. The small capsular bag size may also not permit adequate space for safe implantation. Therefore, very microphthalmic eyes or eyes with poorly formed anterior segment are not good candidates for primary IOL implantation. Mild to moderate microphthalmia does not necessarily preclude IOL placement at the time of cataract surgery. UBM could be used as a tool to help to measure capsular bag diameter directly preoperatively in small eyes to assess the safety margin for IOL implantation. This is useful because we do not need to exclude all patients with small eyes from primary IOL implantation, given the benefit IOL implantation provides in reducing the risk of amblyopia.

Another parameter of the cornea that can be explored in the paediatric population is central cornea thickness (CCT) which is best measured with a pachymeter. However, this instrument is not portable. It has been shown in a previous study that CCT is associated with the visual field loss seen in primary open-angle patients (Mushawiahti et al. 2011). It has a role more for management of the post-operative complication of lens removal in paediatric patients for whom intraocular lens was not implanted namely aphakic glaucoma, rather than during the preoperative evaluation of patients for lens selection.

Although UBM is a useful imaging machine, it is an expensive tool and not readily available in most centres. The operation of the UBM machine also needs considerable expertise. It is costly, time-consuming and relatively inconvenient to perform. Since we found that both corneal diameter and age are predictors for lens diameter, and age has a stronger correlation compare to WTW corneal diameter, we could estimate lens diameter using age combined with WTW measurements as an alternative to direct measurement of the lens diameter with a high-frequency UBM device.

In this study, linear regression test

was used to produce a formula to predict the horizontal lens diameter in children less than four years old. Based on the result of this study, the lens diameter can be calculated by using this model equation:

Lens diameter [mm] = 7.01 + 0.021 Corneal diameter [mm] + 0.028 Age [months]

This model of equation can predict 52% of the factors that affect lens diameter (r^2=0.52). Based on previous studies, (Graybill 1961; Lambert et al. 2019; Solebo et al. 2018) the empty lens capsular bag diameter postsurgical evacuation can be predicted as lens diameter + 1 mm.

This study has several limitations. First is the bias introduced by recruitment of consecutive patients that fulfilled the inclusion criteria for EUA during the study period only. The patient had to have an indication to perform EUA, including abnormality in one of their eyes suspected or confirmed to undergo risks of anaesthesia in such young children. The patient's eyes were dilated for EUA purpose while lens diameter was measured with UBM in the operation theatre. This pupillary mydriasis meant that during EUA the conditions were not exactly physiological, and this might not reflect the exact lens diameter. Furthermore, only the horizontal lens diameter was measured in this study. The vertical lens diameter was not measured due to interference from the eyelids. Therefore, these measurements might not represent the overall lens diameter.

Lens diameter needs to be measured in its horizontal cross-section as accurately as possible. This is because if the recorded image by UBM were not at its precise horizontal cross-section, the lens diameter would be underestimated. Although, we chose the most extensive lens diameter represented by the cross-section that has the largest pupil size from the recorded cross-sectional video, there might still be an error.

The intraobserver and interobserver reproducibility of image measurement obtained during UBM was not evaluated in this study. The variability of the measurement could be subject to a different interpretation of visualised anatomic landmarks. Different observers may set different reference points when measuring. This variability of measurement is another limitation of the study.

The operation of UBM is costly, needs considerable expertise, time-consuming and inconvenient to perform in a routine clinical setting. The transducer requires special preparation, and the operator needs to be familiar with the programs that are designed explicitly for UBM. The complexity of the technique using UBM in the operation theatre is also a limiting factor.

Besides, from this study, a strong claim on the relationship between corneal and lens diameter cannot be made because of the small sample size and the narrow age distribution. The corneal diameter and lens diameter that was obtained from this study also may not represent the local population data given the small sample size. Also, although the eyes that were examined in our study had no known ocular pathology, it might have a subclinical abnormality that was undetected during the time of examination. For instance, the intraocular pressures (IOPs) were measured once as part of the examination under anaesthesia procedure that 11 patients in this study underwent and not formally measured as part of the study protocol in the different subjects. A more reliable method is to monitor the IOP continuously at other time points throughout the day because in glaucoma patients, the IOP fluctuates widely (Ramakrishnan et al. 2019). This recommendation to check IOP continuously is very challenging for a paediatric subject. Therefore, it remains possible that the subjects recruited were not representative of normal eyes in the children population.

In conclusion, we have introduced the application of UBM in measuring capsular bag size directly preoperatively in children from an Asian population. We also demonstrated a relationship between external WTW corneal diameter and lens diameter, albeit not a strong relationship. Therefore, it is not a preferred practice to just rely on the corneal diameter to decide on IOL implantation in small children because the lens diameter does not solely depend on corneal diameter, but other factors such as age and axial length also play an essential role. This fact is essential to be shared with our readers, who may be considering lens implantation in young Asian children. Pediatric patients are difficult to examine, and data for reference is challenging to come by in this population. Hence, the values and observations made in this small scale study we hope may be useful.

We suggest that in a centre equipped with the UBM machine, direct measurement of the lens diameter with UBM before the operation could improve the accuracy of capsular bag diameter estimation and therefore assess the safety margin to implant IOL in small eyes. In a centre where UBM is not available, the regression formula could help to determine the lens diameter. However, it can only predict 52% of the factors that affect the lens diameter. Therefore, it is safer to defer IOL implantation in smaller children with tiny eyes.

Future studies with a larger sample are needed to give a more reliable result and may help to eliminate the confounding factor of multiethnicity. More children less than one year or perhaps less than six months of age should be recruited as these groups of patients have more controversy to decide on IOL implantation. Adult patients could be included as a control arm to look for the lens dimension discrepancy between adults and children. The comparison would be better and more reliable if the measurement was done using the same device in the same study.

The lens diameter should be measured without dilatation to provide a accurate dimension of the lens in its physiologic state. Besides corneal diameter and age, other parameters such as axial length should be measured to help to develop a regression formula which has more reliable predictability as evidenced by previous studies.

Future studies could apply UBM to look at the capsular bag in children's eyes post IOL implantation and assess the behaviour of adult size IOL in small children's eyes. These could help to clear our doubt on how adult size IOLs affects the small capsular bag and the internal ocular structures in smaller eyes. The result of this study will aid the ophthalmologists in the management of pediatric cataracts. Further studies are also needed to evaluate the inter-observer repeatability and agreement of the measurement methods to clarify the result and their reproducibility.

CONCLUSION

There is a moderate positive relationship between corneal diameter and lens diameter. Lens diameter has a strong positive correlation with age in our pediatric population. UBM can be used to measure lens capsular bag size directly preoperatively.

ACKNOWLEDGEMENT

The authors would like to acknowledge the grant provided to project number NMRR-09-974-4858 by the Ministry of Health Malaysia.

REFERENCES

Ashaye, A.O., Olowu, J.A., Adeoti, C.O. 2006. Corneal diameters in infants born in two hospitals in Ibadan, Nigeria. *East Afr Med J* **83**(11): 631-6.

Dong, E.Y., Joo, C.K. 2001. Predictability for proper capsular tension ring size and intraocular lens size. *Korean J Ophthalmol* **15**(1): 22-6.

Bluestein, E.C., Wilson, M.E., Wang, X.H., Rust, P.F., Apple, D.J. 1996. Dimensions of the pediatric crystalline lens: implications for intraocular lenses in children. *J Pediatr Ophthalmol Strabismus* **33**(1): 18-20.

Fea, A.M., Annetta, F., Cirillo, S., Campanella, D., De Giuseppe, M., Regge, D., Grignolo, F.M. 2005. Magnetic resonance imaging and Orbscan assessment of the anterior chamber. *J Cataract Refract Surg* **31**(9): 1713-8.

Graybill, F.A. 1961. An Introduction to Linear Statistical Models. McGraw-Hill, New York, N.Y.

Guenther, W.C. 1977. Desk calculation of probabilities for the distribution of the sample correlation coefficient. *The American Statistician* **31**(1): 45-8.

Rondeau, M.J, Barcsay, G., Silverman, R.H., Reinstein, D.R., Krishnamurthy, R., Chabi, A., Du, T., Coleman, D.J. 2004. Very high-frequency ultrasound biometry of the anterior and posterior chamber diameter. *JRS* **20**(5): 454-64.

Jain, R., Grewal, D., Gupta, R., Grewal, S.P.S. 2006. Scheimpflug imaging in late capsular bag distension syndrome after phacoemulsification. *Am J Ophthalmol* **142**(6): 1083-5.

Kawamorita, T., Uozato, H., Kamiya, K., Shimizu, K. 2010. Relationship between ciliary sulcus diameter and anterior chamber diameter and corneal diameter. *J Cataract Refract Surg* **36**(4): 617-24.

Khng, C., Osher, R.H. 2008. Evaluation of the relationship between corneal diameter and lens diameter. *J Cataract Refract Surg* **34**(3): 475-9.

Kim, K.-H., Shin, H.-H., Kim, H.-M., Song, J.-S. 2008. Correlation between ciliary sulcus diameter measured by 35 MHz ultrasound biomicroscopy and other ocular measurements. *J Cataract & Refract Surg* **34**(4): 632-7.

Kiskis, A.A., Markowitz, S.N., Morin, J.D. 1985. Corneal diameter and axial length in congenital glaucoma. *Can J Ophthalmol* **20**(3): 93-7.

Kohnen, T., Thomala, M.C., Cichocki, M., Strenger, A. 2006. Internal anterior chamber diameter using optical coherence tomography compared with white-to-white distances using automated measurements. *J Cataract Refract Surg* **32**(11): 1809-13.

Lambert, S.R., Aakalu, V.K., Hutchinson, A.K., Pineles, S.L., Galvin, J.A., Heidary, G., Binenbaum, G., VanderVeen, D.K. 2019. Intraocular lens implantation during early childhood: A report by the American Academy of Ophthalmology. *Ophthalmology* **126**(10): 1454-61.

Mashige, K.P. 2013. A review of corneal diameter, curvature and thickness values and influencing factors*. *African Vision and Eye Health* **72**(4): 185-94.

Modesti, M., Pasqualitto, G., Appolloni, R., Pecorella, I., Sourdille, P. 2011. Preoperative

and postoperative size and movements of the lens capsular bag: Ultrasound biomicroscopy analysis. *J Cataract Refract Surg* **37**(10): 1775-84.
Müller, A., Doughty, M.J. 2002. Assessments of corneal endothelial cell density in growing children and its relationship to horizontal corneal diameter. *Optom Vis Sci* **79**(12): 762-70.
Mushawiahti, M., Syed Zulkifli, S.Z., Aida Zairani, M.Z., Faridah, H. 2011. Relationship between central corneal thickness and severity of open angle glaucoma using Optical Coherence Tomography. *Med & Health* **6(**2): 107-13.
Oh, J., Shin, H.-H., Kim, J.-H., Kim, H.-M., Song, J.-S. 2007. Direct measurement of the ciliary sulcus diameter by 35-Megahertz ultrasound biomicroscopy. *Ophthalmology* **114**(9): 1685-8.
Olshan, J.S., Gubernick, J., Packer, R.J., D'Angio, G.J., Goldwein, J.W., Willi, S.M. and Moshang Jr, T. 1992. The effects of adjuvant chemotherapy on growth in children with medulloblastoma. *Cancer* **70**(7): 2013-7.
Pavlin, C.J., Harasiewicz, K., Foster, F.S. 1992. Ultrasound biomicroscopy of anterior segment structures in normal and glaucomatous eyes. *Am J Ophthalmol* **113**(4): 381-9.
Pop, M., Payette, Y., Mansour, M. 2001. Predicting sulcus size using ocular measurements. *J Cataract Refract Surg* **27**(7): 1033-8.
Puvanachandra, N., Lyons, C.J. 2009. Rapid measurement of corneal diameter in children: Validation of a clinic-based digital photographic technique. *J AAPOS* **13**(3): 287-8.
Radhakrishnan, S., Goldsmith, J., Huang, D., Westphal, V., Dueker, D.K., Rollins, A.M., Izzat, J.A., Smith, S.D. 2005. Comparison of optical coherence tomography and ultrasound biomicroscopy for detection of narrow anterior chamber angles. *Arch Ophthalmol* **123**(8): 1053-9.
Ramakrishnan, G., Che Hamzah, J., Sharanjeet-Kaur, S. 2019. Various ways of continuous intraocular pressure monitoring in glaucoma patients: A narrative review. *Med & Health* **14**(2): 17-29.
Richburg, F.A., Sun, H.S. 1983. Size of the crushed cataractous capsule bag. *J Am Intraocul Implant Soc* **9**(3): 333-5.
Solebo, A.L., Cumberland, P., Rahi, J.S. 2018. 5-year outcomes after primary intraocular lens implantation in children aged 2 years or younger with congenital or infantile cataract: findings from the IOL under 2 prospective inception cohort study. *Lancet Child Adolesc Health* **2**(12): 863-71.
Strenk, S.A., Semmlow, J.L., Strenk, L.M., Munoz, P., Gronlund-Jacob, J., DeMarco, J.K. 1999. Age-Related Changes in Human Ciliary Muscle and Lens: A Magnetic Resonance Imaging Study. *Invest Ophthalmol Vis Sci* **40**(6): 1162-9.
Vass, C., Menapace, R., Schmetterer, K., Findl, O., Rainer, G., Steineck, I. 1999. Prediction of pseudophakic capsular bag diameter based on biometric variables. *J Cataract Refract Surg* **25**(10): 1376-81.
Wilson, M.E., Apple, D.J., Bluestein, E.C. and Wang, X.H. 1994. Intraocular lenses for pediatric implantation: biomaterials, designs, and sizing. *J Cataract Refract Surg* **20**(6): 584-91.
Wilson, M.E., Trivedi, R.H. and Pandey, S.K. eds. 2005. Pediatric Cataract Surgery: Techniques, Complications, and Management. Lippincott Williams & Wilkins.
Zar, J.H. 1999. *Biostatistical Analysis*. Pearson Education India.
Zare, M.A., Eshraghi, B., Kiarudi, M.Y., Masoule, E.A. 2011. Application of ultrasound biomicroscopy in the planning of cataract surgery in anterior megalophthalmos. *Indian J Ophthalmol* **59**(5): 400-2.

Received: 12 Apr 2020
Accepted: 06 Aug 2020