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ORIGINAL PAPER

The impact of late-treated pediatric cataract on intraocular pressure

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Abstract
Purpose To assess the intraocular pressure and visual acuity before and after pediatric congenital cataract surgery performed at a relatively older age.
Methods A retrospective analysis of all consecutive pediatric patients diagnosed and operated for bilateral congenital cataracts during a seven-year period (2012–2018) in rural southern Ethiopia. Non-ambulatory vision was defined as hand motion or worse. The main outcome measures were intraocular pressure (IOP) and visual acuity.
Results Thirty-two children were included, 17 females (53.1%), with a mean age of 11 years (± 2.83) [range, 7–18]. A total of 59 eyes were operated on. The mean follow-up was 4.8 ± 1.8 years (range, 2–8). VA improved from 20/1400 preoperatively to 20/440 postoperatively OD and 20/540 OS ($p < 0.001$). More eyes had ambulatory vision after cataract surgery than pre-surgery (56 eyes [95%] vs. 29 eyes [49%], $p < 0.001$). The IOP decreased from a mean preoperative value of 18.4 ± 7.1 mmHg to 14.5 ± 2.9 postoperatively OD ($p < 0.001$) and 16.3 ± 5.9 mmHg to 13.9 ± 3.5 OS ($p < 0.001$). Fifteen eyes (24%) had increased IOP (> 21 mmHg) preoperatively, of which three remained high after surgery. Positive correlations were found between IOP, axial length and cup-to-disc ratio. None of the patients required pressure-lowering procedures.
Conclusion Bilateral congenital cataracts may be associated with ocular hypertension, with possible progression to glaucoma if left untreated. Surgery at a relatively older age often was associated with a significant improvement in intraocular pressure and ambulatory vision.

Keywords Pediatric glaucoma following cataract surgery · Pseudophakic glaucoma · Congenital cataract

Introduction

Congenital cataract is a rare disease with an estimated prevalence of 0.6 to 6.0 per 10,000 children [1]. Bilateral cases consist of about half of the childhood cataract cases [2], and are one of the most common treatable causes of childhood blindness globally [3, 4]. Around half of the bilateral cases are familial [5, 6]

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and constitutes a significant source of visual impairment in low-income countries with limited medical availability [7].

Project "Eye-opener" was initiated in Ethiopia in 2012 in an effort to find children with unoperated bilateral mature cataracts (presumed to be congenital in nature) and provide them with surgical treatment. Our cohort mainly consisted of children in schools for the blind with isolated bilateral congenital cataracts. We operated on both eyes and studied their ability to acquire various visual functions, as described in previous reports [8–10].

Pediatric glaucoma following cataract surgery (GFCS) [11], previously called pseudophakic or aphakic glaucoma, is a potentially blinding disease, described in 2% to 41% of the cases [12–18]. The exact mechanism of GFCS remains unknown [17, 19]. This study allowed for assessing the incidence of ocular hypertension and glaucoma before and after cataract removal surgery in congenital cases that were treated years after birth. Additionally, we were able to measure the effect of this late procedure on visual acuity. The purpose of this article was to investigate pre- and postoperative ranges of intraocular pressure noted in cases of presumed congenital cataract with delayed surgery.

Methods

A retrospective analysis of all consecutive pediatric patients diagnosed and operated for bilateral congenital cataracts during a seven-year period (2012 to 2018) in rural southern Ethiopia.

Patients

Most patients were recruited from schools for the blind in all areas of Ethiopia, and some from community referrals. All patients had bilateral, visually significant, isolated congenital cataracts (Fig. 1). The diagnosis was based on standard clinical assessments, positive family history when available, and the presence of sensory nystagmus. Genetic testing for bilateral cataract evaluation was not available in this rural setting. This study adheres to the Declaration of Helsinki and was approved by the regional institutional ethics review board (IRB) of the Hebrew University in Jerusalem and Hawassa University, Ethiopia. Informed consent was obtained from all participants.

The following data were abstracted from the medical records: visual acuity (VA), horizontal corneal diameter (HCD) measurements, IOP, and cup-to-disc ratio (CDR) assessments. CDR was assessed postoperatively as the cataracts precluded posterior pole view. VA was measured with the aid of a local translator to the tribal language. The IOP was measured using the Tono-Pen XL (Reichert, Depew, NY). Non-ambulatory vision was defined as hand motion or worse.[16] The postoperative IOP was measured as an average of twice-yearly measurements over the entire follow-up period.

All procedures were performed by one of two experienced pediatric ophthalmology surgeons at Hawassa University Referral Hospital.

Statistical analysis

Statistical analysis was performed using a paired-sample t test to evaluate pre- and postoperative data such as visual acuity and IOP. A χ^2 test was used to evaluate changes in ambulatory vision rates. Pearson's bivariate correlation was used to analyze correlations between age, IOP, axial length, cup to disc ratio, and visual acuity. The statistical analysis was performed for each eye separately rather than including all eyes to prevent biased results due to inter-eye correlation [20]. Statistical analysis was performed using SPSS (version 26, SPSS Inc., Chicago, IL). All results are presented as mean values ± standard error of mean. Snellen visual acuity findings were converted to logarithm of minimal angle of resolution (LogMAR) values.

Results

Demographics

Thirty-two consecutive patients (17 females, 53%) underwent 59 cataract surgeries, with 27 patients having bilateral surgery (simultaneous or consecutive). The average age at surgery was 11.06 ± 2.83 years (range 7–18 years). Five patients with bilateral cataracts underwent unilateral surgery due to the surgeon's (I.B.Z.) estimate of low vision potential in the non-operated eye. The average follow-

Fig. 1 Clinical photograph of a 12-year-old female patient presenting with bilateral congenital cataract, exotropia, and sensory nystagmus

up time was 4.8 ± 1.8 years (range 2–8 years). Demographics of the study population are summarized in Table 1.

Ocular indices

The mean axial length (AXL) was 22.99 ± 1.08 mm OD (range 20.15–24.8) and 22.91 ± 1.07 mm OS (range 20.70–25.1). The mean cup-to-disc ratio (CDR)

Table 1 Demographic and clinical characteristics of 32 pediatric patients who underwent cataract extraction in southern Ethiopia

Variable	Description	Data	
Total patients	(n)	32	
Gender	Female	17	
	Male	15	
Age at surgery	(Years)	Mean 11.06 ± 2.83 SD	Range 7–18
Operated eyes	OD	30	
	OS	29	
	Bilateral	27	
	Total	59	
Axial length (mm)	OD	Mean 22.99 ± 1.08	Range 20.15–24.8
	OS	Mean 22.91 ± 1.07	Range 20.70–25.1
Cup to disc ratio	OD	0.41 ± 0.16	0.2–0.9
	OS	0.37 ± 0.12	0.2–0.6
Follow-up	(Years)	Mean 4.8 ± 1.8	Range 2–8
		OD	OS
Cataract type	Nuclear Sclerosis + 3	6 (18.8%)	5 (15.6%)
	Mature	20 (62.5%)	19 (59.4%)
	Complicated*	2 (6.3%)	3 (9.4%)
	PSC	0 (0%)	1 (3.1%)
	Partially absorbed	3 (9.4%)	3 (9.4%)
	Not documented	1 (3.1%, pre-phthisis)	1 (3.1%, RD)
	Total	32	32
Cornea	Normal	20 (61.5%)	23 (71.9%)
	Microcornea	11 (34.4%)	9 (28.1%)
	Not documented	1 (3.1%)	0
	Total	32	32

Ant vit, anterior vitrectomy, *PCIOL*, posterior chamber intraocular lens, *PSC*, posterior subcapsular, *RD*, retinal detachment, *SD*, standard deviation, *mm*, millimeters

*Complicated—capsule-iris adhesions

as assessed postoperatively was 0.41 ± 0.16 OD (range 0.2–0.9) and 0.37 ± 0.12 OS (range 20.70–25.1). A large percentage of the eyes (11 (34%) OD, 8 (25%) OS) had microcorneas defined as a horizontal corneal diameter < = 10 mm. All patients but one had nystagmus attributed to severe visual impairment (sensory nystagmus).

Visual acuity

Visual acuity (VA) improved from 20–1400 preoperatively to 20–440 postoperatively OD ($p < 0.001$, Paired-samples *t* test) and from 20/1400 to 20/540 OS ($p < 0.001$, Paired-samples *t* test) (Table 2). Improvements in VA remained significant when compared using modified ambulatory categories: among the 59 operated eyes, 30 (50.8%) eyes had non-ambulatory vision preoperatively, defined as hand motion or worse. Postoperatively, three (5.1%) eyes had non-ambulatory vision ($p < 0.001$, χ^2, Fig. 2). None of the eyes deteriorated to non-ambulatory vision if they started with ambulatory vision preoperatively.

Cataract classification and procedure

Most cataracts were mature (39, 60.9%), followed by advanced nuclear cataracts (11, 17%). Six (9.3%) cases had partially absorbed cataracts. Five (7.8%) cases were complicated with capsule-iris adhesions. One cataract (3.1%) was posterior subcapsular (PSC).

The surgical technique was small-incision manual extracapsular cataract extraction [21] in 51 eyes, and nine eyes underwent clear cornea incision cataract extraction. Posterior capsulotomy was performed on the younger cases and when the capsule was opaque, fibrous, or adhered to the anterior capsule. Anterior vitrectomy was performed in 45 eyes (Alcon Vitrectomy Accurus 200). Fifty-five eyes underwent posterior chamber IOL implantation, and the remaining four eyes were left aphakic. Bilateral cases which were operated on simultaneously were performed under general anesthesia. Unilateral procedures were performed under either general anesthesia, or local anesthesia in cooperative patients. None of the patients developed endophthalmitis postoperatively. No other

Table 2 Visual acuity and intraocular pressure of 32 pediatric patients who underwent cataract extraction

Variable	Description				
		Mean	Range	SD	*p*-value
VA (LogMar)	OD pre-op	1.85	1.0–2.2	0.33	
	OD post-op	1.34	0.6–1.9	0.41	< 0.001**
	OS pre-op	1.84	1.0–2.2	0.32	
	OS post-op	1.43	0.78–1.6	0.29	< 0.001**
		Non ambulatory (n)	Ambulatory (n)	Ambulatory (%)	
VA—ambulation	OD pre-op	15	15	50%	
	OD post-op	3	27	90%	0.002†
	OS pre-op	15	14	48.3%	
	OS post-op	0	29	100%	< 0.001†
	Total pre-op	30	29	49.2%	
	Total post-op	3	56	94.9%	< 0.001†
		Mean	Range	SD	
IOP (mmHg)	OD pre-op	18.44	7–34	7.13	
	OD post-op	14.55	9–22	2.94	< 0.001**
	OS pre-op	16.28	6–32	5.93	
	OS post-op	13.9	6–22	3.58	< 0.001**

**SD*, standard deviation; *VA*, visual acuity; *IOP*, intraocular pressure; *pre-op*, preoperative; *post-op*, postoperative

**Paired-sample *t* test before and after cataract extraction, same eye

†Chi-square test

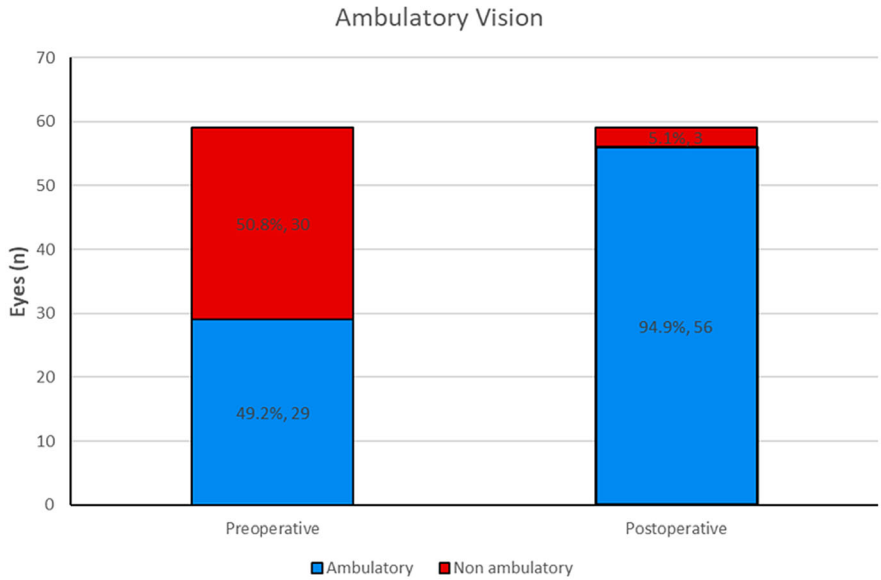

Fig. 2 Visual acuity changes after surgery of 59 eyes in 32 pediatric patients who underwent cataract extraction in southern Ethiopia. Non-ambulatory vision was defined as hand motion or worse and ambulatory vision as following objects or better. The percentage of ambulatory visual acuity increased among eyes after surgery from 49.2 to 94.9%. *$p < 0.001$, $\chi 2$ test*

complications were encountered, and no secondary procedures were performed.

Intra ocular pressure (IOP)

The mean preoperative IOP was 18.44 ± 7.13 mmHg (range 7–34) for the right eye and 16.28 ± 5.93 mmHg (range 6–32) for the left. Fifteen (24%) eyes had increased IOP preoperatively, defined as IOP > 21 mmHg. Postoperatively, IOP decreased to 14.55 ± 2.94 (range 9–22) OD and to 13.9 ± 3.58 (range 6–22) OS ($p < 0.001$ for each eye, paired-samples t test). The average decrease in IOP was 4.25 ± 4.62 mmHg in the right eye (95% CI 2.56–5.95, $p < 0.001$) 3.0 ± 3.44 mmHg in the left (95% CI 1.71–4.28, $p < 0.001$ OS). There was a significant positive correlation between pre- and postoperative IOP for each eye (Pearson's bivariate correlation, Fig. 3). Three eyes had increased IOP (> 21 mmHg) postoperatively. These cases had higher IOP measurements preoperatively (32–34 mmHg). The CDRs in these patients were 0.5, 0.9, and undocumented for the third. Two of these patients required topical anti-glaucoma medications. They were treated with timolol–acetazolamide during the follow-up period with normalization of IOP. No patient required pressure-lowering procedures (Table 2). None of the eyes with IOP in the normal range preoperatively developed postoperative OH or glaucoma.

Positive correlations were found between preoperative IOP and CDR (OS: 0.8, $p < 0.001$; OD: 0.7, $p < 0.001$), axial length (OS: 0.6, $p < 0.001$; OD: 0.3, $p = 0.051$), as well as postoperative IOP and CDR (OS: 0.5, $p = 0.012$, OD: 0.6, $p < 0.001$), and CDR and AXL (OS: 0.6, $p = 0.003$, OD: 0.4, $p = 0.036$). Postoperative IOP was correlated with AXL for the left eye only (OS: 0.6, $p < 0.001$, OD: 0.2, $p = 0.3$ non-significant).

No correlations were found between patients' age and pre-/postoperative IOP, axial length, and visual acuity. Delta visual acuity and delta IOP were not influenced by gender or by cataract subtype.

Discussion

In 2018, the childhood glaucoma research network (CGRN) published a new classification of childhood glaucoma [11]. They coined the term "glaucoma following cataract surgery" (GFCS) as one of the secondary glaucoma types, and a glaucoma that exists prior to cataract removal was given a different classification. GFCS has a reported incidence of 2–41% and may appear years following cataract surgery [12–19, 22, 23]. Treatment is challenging, often requiring more than one surgical procedure [24].

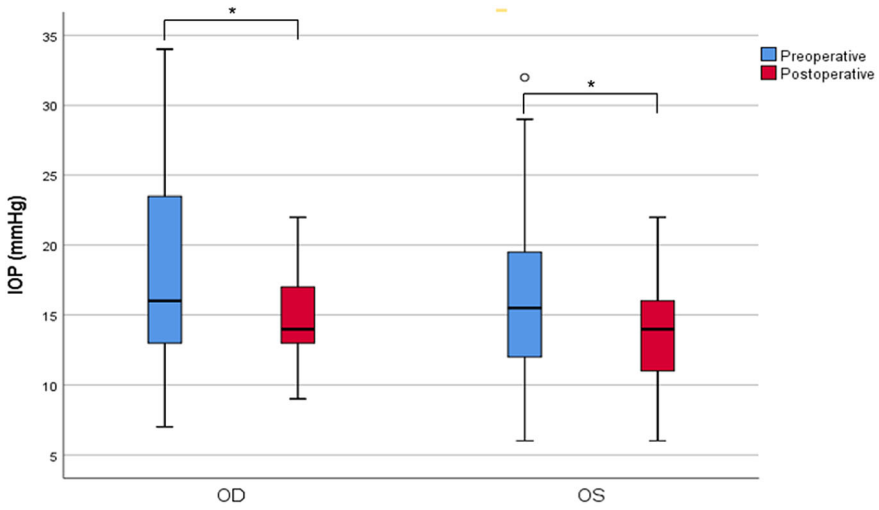

Fig. 3 Intraocular pressure (IOP) changes after surgery for 32 pediatric patients who underwent cataract extraction in southern Ethiopia. The IOP was reduced on average after surgery, from 18.44 to 14.55 mmHg OD and 16.28–13.90 mmHg OS. **p < 0.001, paired samples t test*

Several hypotheses were proposed for the pathogenesis of GFCS [17, 19] and most can be divided into primary or surgery induced (secondary). The first theory suggests that both the glaucoma and the congenital cataract are manifestations of a single ocular insult [25]. Some patients show anatomical variations in the anterior chamber angle, such as highly pigmented trabecular meshwork or a flat iris plane with a poorly defined scleral spur and ciliary body [13, 19, 25]. However, the normal angle anatomy observed in other patients, and the glaucoma's late onset, weigh against this hypothesis [19].

The second theory suggests that the cataract surgery and the resultant inflammatory response are responsible for the onset of the glaucoma [19]. This can be supported at least in part by the fact that glaucoma may develop years after the operation [19]. In addition, Walton[26] reported gonioscopic observations in patients with childhood aphakic glaucoma, which revealed profound abnormalities considered to be acquired in 96% of eyes with open angles. Further support can be found by the fact that delaying cataract surgery reduces the risk of glaucoma [22]. It is possible that early surgery disrupts the maturation of the trabecular meshwork hence predisposes it to glaucoma or ocular hypertension (OH) [22]. This can occur secondary to trabecular meshwork damage from postoperative inflammation, structural changes to the angle, or deficiency of essential cytokines normally secreted by the crystalline lens [22]. In addition, children are susceptible to steroid-induced OH, which mandates careful monitoring in the perioperative period [27].

Many factors have been reported that increase the risk of GFCS, including: persistent fetal vasculature, fetal nuclear cataracts, microphthalmos, small corneal diameter, retained lens material, chronic inflammation and reoperations [22, 28]. Several of these are interrelated [29]. Studies that examined the role of aphakia as a predisposition factor to GFCS have contradictory findings with inconclusive evidence. [18, 19, 28, 30–33] It is generally agreed that surgery at a lower age poses the greatest GFCS risk, as supported by the findings of the TAPS, IATS, BICCG, PEDIG, and other studies [22, 28, 30, 31, 33, 34].

One way to explore the pathophysiology of GFCS would be to evaluate the long-term natural history of unoperated congenital cataracts and their association with glaucoma. Owing to this study's unconventional and unique setting, we were able to do just that.

In our study, we included children from Ethiopia with limited availability to modern medical facilities. Hence, we were able to find older children with untreated bilateral congenital cataracts (mean 11.06 ± 2.83 years). All eyes were observed for 2–8 years after the operation.

Postoperatively, there was a significant IOP reduction. The incidence of OH (IOP > 21) decreased from 24% to 4.8% postoperatively. IOP was correlated with CDR and axial length as expected. Since the CDR was measured postoperatively, along with up to a single AXL measurements was documented per patient, eyes with preoperative OH could only be diagnosed as

suspected glaucoma rather than definite glaucoma [11]. Having said that, as the preoperative IOP was strongly correlated with CDR (CC 0.7–0.8, $p < 0.001$), it is the authors' opinion that at least some of these cases had glaucoma. This is in line with previous reports' definitions of pediatric glaucoma [16, 23].

Primary Pediatric Glaucoma and Congenital Cataract

The incidence of primary glaucoma in the pediatric population varies with ethnicity, ranging from 1:2,500 to 1:18,500 live births for primary congenital glaucoma (PCG), and less than that for juvenile glaucoma [35]. The incidence of primary glaucoma in patients with congenital cataracts is unknown. However, a recent study examined the incidence of cataract in PCG [36]. They retrospectively reviewed 108 PCG cases, and found a high incidence (16.2%) of cataract extractions, during an average 8 years of follow-up. However, these cataracts were associated with previous pressure lowering procedures. Also, in cases of buphthalmos due to advanced PCG, there is a risk of zonules rupture and cataract [37].

Hennig et al. described outcomes of cataract removal for 390 children from Nepal and northern India [38]. The mean age was 7.4 ± 4.0 years, range 0.5–15. They didn't describe preoperative IOP, yet found that postoperative glaucoma was rare (< 1%).

One explanation for the high preoperative OH rate demonstrated in our series (24%) would be lens-induced, attributable to either phacolytic or phacomorphic underlying mechanisms [35]. The postoperative IOP decrease observed in our patients supports this explanation. Yet, IOP decrease following cataract surgery is common in non-glaucomatous eyes as well, and is proportional to the initial IOP [39–41]. As our patients were operated on at a mean age of 11 years, it is not surprising that none of the children developed secondary postoperative glaucoma, as is the case with adult cataract surgery and lowering of the IOP post-surgery [39–41].

A second explanation would be that the preoperative OH represents primary pediatric glaucoma, most probably the juvenile subtype (as our patients did not have characteristic PCG findings such as buphthalmos or Haab stria). Such an association between primary glaucoma and congenital cataracts suggests a common ocular origin. This would support the theory uniting both glaucoma and congenital cataracts as manifestations of a single ocular syndrome. Naturally, any combination of these explanations is also possible.

Visual acuity

We found a statically significant improvement in visual outcome, both when measured by LogMar and by ambulatory vision, defined as following objects or better. Patients were significantly more likely to have ambulatory VA after the operation. This is supported by previous findings of our group [8, 10, 42] as well as others [38, 43], describing pediatric cataract extractions at a later age in developing countries. We conclude that even in a setting of late presentation and limited resources, cataract surgery has mostly beneficial visual outcomes.

Limitations

The main limitations of this study stem from its retrospective nature, and from paucity of imaging and advanced clinical testing data due to its rural setting. Examinations such as gonioscopy, pachymetry, UBM, OCT, and visual fields were not performed in this setting. As previously discussed, this limits our ability to identify all cases of preoperative glaucoma, and to characterize the anterior chamber angle. We presumed the cataracts in our cohort to be congenital due to the cataract morphology, deep amblyopia with sensory nystagmus, positive family history and past medical history when available. The patients had no prior medical documentation specifying the cataract onset.

Our patients represent a unique subpopulation, which might differ in several aspects from the western pediatric population, on which current medical literature commonly relies upon. First, all our patients had bilateral congenital cataracts, which might indicate a genetic predisposition with a distinct long-term natural history. Second, the African descent of our patients might add genetic factors that differ from the western pediatric population. Third, the older age of these patients might be associated with a reduced inflammatory response, hence a lower rate of postoperative IOP increase. Thus, inferring from our findings to the general western pediatric population should be done with caution.

In conclusion, bilateral congenital cataracts are possibly associated with increased IOP and glaucoma if left untreated. In addition, congenital cataract extraction performed at an older age is associated with a significant improvement in visual outcome. Further research is needed to better understand the relation between pediatric glaucoma and congenital cataract.

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Compliance with Ethical Standards

Conflict of interest None of the authors have any conflicts of interest.

Human or Animal Participants This study adheres to the Declaration of Helsinki and was approved by the regional institutional ethics review board (IRB) of the Hebrew University in Jerusalem and Hawassa University, Ethiopia.

Informed consent Informed consent was obtained from all participants.

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