Pediatric Glaucoma in a University Hospital

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Abstract

Aims and objectives: This study aimed at describing the characteristics and outcomes of pediatric glaucoma patients in a university hospital in Lebanon and comparing them between primary congenital glaucoma (PCG) and secondary glaucoma.

Materials and methods: Sixty-four eyes of 40 pediatric glaucoma patients with a follow-up of 1 year or more were reviewed. Parameters were studied for both PCG and secondary glaucoma groups. Three major outcomes were considered: intraocular pressure (IOP) control, final best-corrected visual acuity (BCVA), and the proportion of failed angle surgeries.

Results: Sixty-four eyes were included divided into 29 PCG and 35 secondary glaucoma eyes, followed up for a mean of 6.6 ± 4.7 years. Eyes with PCG presented earlier, with a higher initial IOP and underwent earlier surgery than their secondary glaucoma counterparts. Although 85.9% of all eyes achieved good IOP control, 44.4% of them had a BCVA ≥20/50 with PCG having a better visual prognosis. Secondary glaucoma eyes needed more medications at the end of their follow-up. In this group, it was shown that a later age at first surgery, unilateral disease, and multiple surgeries were associated with a BCVA < 20/50.

Conclusion: Patients with PCG presented earlier and with a higher IOP than secondary glaucoma; they were also operated on earlier. Both groups demonstrated good IOP control at the end of the follow-up period with PCG eyes having a superior visual outcome. Secondary glaucoma eyes required a higher number of medications at their final visit. In this population, multiple surgeries, unilateral disease, and a delayed first surgery conferred a poorer visual prognosis.

Clinical significance: Data regarding the characteristics of pediatric glaucoma, especially in the Middle East, are scarce. Our study sheds the light on the presentation of different types of pediatric glaucoma and their outcomes namely IOP control and visual acuity.

Keywords: Congenital glaucoma, Glaucoma surgery, Intraocular pressure, Pediatric glaucoma, Retrospective chart review, Visual acuity.

Journal of Current Glaucoma Practice (2021): 10.5005/jp-journals-10078-1291

Introduction

Pediatric glaucoma is a relatively rare condition that frequently results in visual impairment.[1] It is usually classified as primary, secondary, or acquired.[1] The primary form includes two major categories depending on the age of onset. It is termed primary congenital glaucoma (PCG) if it presents in the first 4 years of life, and juvenile primary open-angle glaucoma if it occurs after that age.[2] The primary congenital form is the most common form of pediatric glaucoma and is also the most responsive to treatment.[2–6] It is more common in males and accounts for 0.01–0.04% of blindness.[7] Secondary glaucoma is frequently due to congenital conditions (such as aniridia and aphakia) or various syndromic disorders, whereas acquired glaucoma typically arises from non-congenital factors such as inflammation and drugs.[1,2]

Several studies have published data on the epidemiologic and prognostic factors of PCG. It is 4 times more common in the Middle East than the West, and in Saudi Arabia, it is the cause of 16% of childhood blindness.[8] This could be attributed to the increased proportion of consanguineous marriages in this region of the world.[9] A study carried out on the demographics of congenital glaucoma in the West Bank and Gaza Strip showed that 49% of patients had consanguineous parents.[10] Additionally, the incidence of congenital glaucoma and its genetic mutations vary by ethnicity; mutations in the cytochrome P450 gene CYP1B1 were found in 50% of patients affected with PCG worldwide.[11] However, this frequency varies in different populations. Our group showed that the percentage of CYP1B1 mutations in the Lebanese population was 33%,[12] while in neighboring countries such as Saudi Arabia and Israel, it was 100%[13] and 80%,[14] respectively. This is probably due to the genetic heterogeneity of the Lebanese population.[12]

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The prognosis of the disease seems to be linked to several factors including age at initial presentation, time of first surgery, the extent of optic nerve injury, presence of other ocular comorbidities, corneal size, and the development of anisometropia/amblyopia.[15] Despite all the above variables, a study on 25 Arab-Bedouin children with PCG in 2005 reported presenting intraocular pressure (IOP) to be the only independent predictor of failure of treatment when success was measured as IOP >5 and <21 mm Hg at the end of a 2-year period, off medication, regardless of the number of procedures they underwent.[16]

The visual prognosis of PCG seems to be satisfactory with 52–79% of patients having a final visual acuity of 20/50 or better.[17] Other types of glaucomas including secondary glaucoma seem to have worse prognosis.[17] Factors that confer a bad visual prognosis include neonatal onset, unilaterality, poor vision at the time of diagnosis, and undergoing numerous procedures.[18,19] The treatment of the condition is usually surgical with angle surgery, trabeculotomy, and goniotomy being among the most commonly

performed procedures in these patients.[20] The proportion of children who respond to medical treatment is generally lower than it is in the adult population.[21]

There is a relative lack of data on pediatric glaucoma in the region, and in Lebanon specifically. This paper aimed to report the characteristics of the affected population in Lebanon and to compare results with previously published studies in terms of demographics, surgical interventions, outcomes, and prognostic factors.

MATERIALS AND METHODS

This was a retrospective chart review of pediatric glaucoma patients who presented to the ophthalmology department at the American University of Beirut Medical Center (AUBMC) over a span of 19 years (from January 1, 2000, to January 31, 2019). This list was gathered from hospital medical records using both surgery billing codes (trabeculectomy, goniotomy, trabeculectomy, and glaucoma shunt surgery) and ICD 9 codes. The study was approved by the Institutional Review Board (IRB) at the American University of Beirut and consent was waived. Furthermore, it abided by the principles stated in the Declaration of Helsinki. Demographic variables included age, gender, country of origin, and family history of glaucoma. Visit parameters recorded included date, age at presentation and first surgery, type of glaucoma and laterality, IOP and method of assessment, visual acuity, cup-to-disk ratio, current medications, surgical procedures, and complications. Parents of patients who reported themselves to be related were marked as consanguineous. Additionally, family history was marked positive if at least one family member was diagnosed with glaucoma. Most patients underwent sequential examinations under anesthesia where IOP was measured with a Tonopen XL (Reichert, Depew, New York, USA) or a Perkins tonometer (Clement Clarke, UK). They also underwent anterior segment examination, gonioscopy, axial length, and corneal diameter measurements and when possible, fundoscopy and retinoscopy. This information would complement any missing information from the clinic visit (largely due to the difficulty of examining a crying/agitated child).

Primary outcomes included: adequate IOP defined as a value <21 mm Hg (with or without medication) at the end of the follow-up period and good visual outcome defined as a best-corrected visual acuity (BCVA) of 20/50 or better. Angle surgery (goniotomy/trabeculotomy) was considered successful if the respective eye did not require re-operation. Anisometropia was defined as an interocular refractive error difference of ≥3 diopters for myopia, ≥1.5 diopters for hyperopia, and ≥2 diopters for astigmatism.

Analysis

Our chart review revealed a total of 40 patients (64 eyes) that had a follow-up of at least 1 year. Glaucomas were classified, as per the World Glaucoma Association,[22] into either primary or secondary glaucomas. Primary glaucoma included PCG and juvenile open angle glaucoma (JOAG). Secondary glaucoma included aphakic and uveitic glaucoma and glaucoma due to non-acquired conditions such as Sturge–Weber syndrome and aniridia. Surgical procedures and medical therapies were identified and tallied. Surgical procedures included trabeculotomy, trabeculectomy with mitomycin C (MMC), cyclophotocoagulation, and Ahmed tube insertion while medical therapy included beta-blockers, prostaglandins, alpha agonists, and topical/oral carbonic anhydrase inhibitors. Trabeculotomy was the first line treatment for most patients with PCG in our center, unless canal of Schlemm could not be identified.[23] In those cases, trabeculectomy (if eye was too small for tube shunt placement) or glaucoma shunt surgery (Ahmed tube) was performed. Cyclophotocoagulation using a diode laser to partially destroy the ciliary body was performed in eyes with worse visual prognosis or when surgical interventions failed to control IOP.[24] Sight-threatening complications of these procedures include hypotony, choroidal detachment, intraocular hemorrhage, retinal detachment, and endophthalmitis.[25]

Statistical Analysis

The extracted data were entered into SPSS V25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp., USA). Means and standard deviations were reported for demographic variables and eye examination parameters in addition to the number of medications and surgeries. As we only had three eyes that were diagnosed with JOAG, these were eliminated from our analyses as they are not numerous enough to be representative of the disease. A p value of 0.05 or less was considered statistically significant.

RESULTS

Demographic and Presenting Variables

Demographic variables and baseline characteristics of the studied eyes are reported in Table 1. Forty patients (64 eyes) were included: 29 eyes (45.3%) had a primary form of glaucoma, while 35 (54.7%) had secondary glaucoma. The most common diagnosis in the primary group was PCG, representing all of the primary cases included in this analysis. The most common type in the secondary group was aphakic glaucoma (45.7%). Other types of secondary glaucoma included uveitic glaucoma (8.6%), post-vitrectomy glaucoma (5.7%), and glaucoma due to Peter's anomaly (5.7%), aniridia (5.7%), and

Table 1: Demographics and baseline characteristics

Type of glaucoma	Primary congenital glaucoma	Secondary glaucoma
N (patients/eyes)	19/29	21/35
Gender ratio (male:female)	1.9:1	1:1.2
Family history of glaucoma, N (%)	4 (13.8)	10 (28.6)
Parent consanguinity, N (%)	10 (34.5)	0 (0.0)
Bilateral involvement, N (%)	20 (69.0)	28 (80.0)
Follow-up duration, years (mean ± SD)	5.6 ± 3.9	7.8 ± 5.2
Age at presentation, years (mean ± SD)	1.6 ± 2.9 [2 days–10 years]	4.7 ± 5.4 [2 days–17 years]
Age at first surgery, years (mean ± SD)	0.6 ± 0.5	3.4 ± 5.2
IOP at presentation, mm Hg (mean ± SD)	31.9 ± 13.5	23.5 ± 6.5
Initial C/D ratio (mean ± SD)	0.4 ± 0.2	0.4 ± 0.3

Table 5: Number of surgeries per eye

	Number of surgeries per eye				
	0 (%)	1 (%)	2 (%)	3 (%)	4 (%)
Primary congenital glaucoma	0 (0.0)	19 (65.5)	8 (27.6)	2 (6.9)	0 (0.0)
Secondary glaucoma	11 (31.4)	9 (25.7)	7 (20.0)	7 (20.0)	1 (2.9)
Pediatric glaucoma (all)	11 (17.2)	28 (43.8)	15 (23.4)	9 (14.1)	1 (1.6)

glaucoma. Our mean follow-up duration was 6.60 years. In the PCG group, there was a greater proportion of parent consanguinity compared to the secondary glaucoma group. Also, patients with PCG presented at a younger age and were operated on earlier than their secondary glaucoma counterparts. Furthermore, they had a significantly higher IOP at presentation. Regarding final outcomes, 85.9% of all studied eyes had good IOP control, while 44.4% of them achieved a final visual acuity of 20/50 or better. Final IOP and cup-to-disk ratios did not differ between groups; however, the final number of medications was higher in the secondary group. Surgeries were distributed differently in the two groups: eyes with PCG underwent more trabeculotomies while secondary glaucoma eyes had more cyclophotocoagulation procedures done. The most commonly performed procedure overall was trabeculectomy (55.4%), followed by Ahmed glaucoma valve implantation (24.3%). All eyes in the PCG group underwent at least one surgery, while over 30% of eyes in the secondary group did not undergo any surgeries and were controlled medically.

Primary congenital glaucoma is believed to be the most frequent type of childhood glaucoma.[26] Our study revealed an almost equal distribution of eyes with respect to these two types of glaucoma (29 eyes with PCG vs 35 with secondary glaucoma). This is in contrast with other studies looking at pediatric glaucoma in referral centers where the largest group was PCG.[27] Several factors may have influenced the increased proportion of secondary glaucoma at our center. First, our center is a referral center and secondary glaucoma usually presents with multiple other comorbidities that may prompt referral. Second, this may also be due to the high levels of consanguinity in our population compared to other populations,[28] and the genetic basis of diseases that cause secondary glaucoma such as anterior segment dysgenesis[29] and post-congenital cataract surgery (aphakic glaucoma).[30]

Age at presentation in PCG eyes followed a similar trend to what was previously reported of presenting earlier than secondary glaucoma but the actual value was larger than what has been previously published. Our mean age at presentation was 1.6 years as opposed to 79% of cases presenting within 12 months of life in a British study[2] and a median age diagnosis of 0.5 years by Saavedra et al.[27] Due to the earlier presentation, it naturally follows that age at first surgery was earlier in PCG.

Presenting IOP in the PCG group was higher than that of secondary glaucoma (31.9 and 23.5 mm Hg, respectively). This is in contrast with what was previously published in a Saudi Arabian study that showed no significant differences between the two groups at baseline.[31] Saavedra et al. reported a higher initial IOP in secondary glaucoma patients with both median values being lower than our means (16 and 20.5 mm Hg, for PCG and secondary glaucoma groups, respectively). However, the initial difference in our population did not seem to affect eventual IOP control. It has previously been reported that IOP at presentation carried no significant association with final IOP at 1 year.[2] With regards to

medications, PCG eyes had fewer medications at follow-up possibly reflecting the better control and prognosis of glaucoma in this group with surgical treatment.[32] A similar trend was demonstrated by Saavedra et al. in a study carried out in Colombia which revealed that over 25% of PCG eyes were medication-free at the end of the follow-up period while in the secondary group this value was at 7.5%.[27]

The visual prognosis in children with glaucoma is correlated with the type of the associated ocular pathology.[17] In a review paper, Beck reported that PCG had the best visual prognosis, with 52–79% having a visual acuity of 20/50 or better.[17] Glaucomas associated with congenital ocular anomalies and secondary glaucomas had a worse visual prognosis, with 30–50% of eyes noted to be 20/50 or better.[3,17,32–34] This study similarly demonstrated the better visual prognosis of PCG eyes compared to secondary glaucoma eyes (59.1 vs 34.4% of eyes achieving a final visual acuity of 20/50 or better in PCG vs secondary glaucoma groups, respectively). Another study from Canada revealed a similar pattern in PCG eyes (77.3% visual acuity equal 20/50 or better with good IOP in all) compared to secondary glaucoma eyes.[32] A study in the US population further reinforced the previous findings.[18]

In our region, similar trends have been reported regarding IOP control as well: a study done in the West Bank on 118 PCG eyes showed that 69% of them had good IOP control at the end of 43.9 months, off medications.[10] Interestingly in our study, the number of eyes reaching good IOP control was quite higher: 86.6% of all studied eyes with or without meds with no significant differences between groups. The inclusion of patients controlled on medications in our definition may have led to the higher reported percentage. With regards to angle surgery outcomes, studies have portrayed similar success rates for trabeculectomy.[34] Fulcher et al. reported a 92.3 and 85.7% success rate for trabeculectomy in primary infantile glaucoma and secondary glaucoma patients, respectively.[34] Our results were comparable for PCG (89.7%) and secondary glaucoma (94.3%).

Our results also revealed that in the PCG group, an increased number of surgeries was associated with poor IOP control. Moreover, in secondary glaucoma, a high presenting IOP was associated with poor IOP control at the end of the follow-up period. With regards to final visual acuity, it was shown that at a later age at first surgery, unilateral disease, and multiple surgeries were associated with a poor BCVA (<20/50). Our results are in concordance with previous studies. Khitri et al. previously reported that pediatric glaucoma patients with the unilateral disease were 5 times more likely to have a poor visual outcome (BCVA < 20/200).[18] Moreover, those who underwent >2 surgeries were 32 times more likely to have visual impairment.[18]

To our knowledge, this is the longest follow-up of patients with PCG and secondary glaucoma in the region at 6.6 ± 4.7 years (24 months in a study from Israel[16] and 43.9 months in West Bank and Gaza[10]) comparing both types of pediatric glaucoma. Further

strengths lie in the fact that our chart review was comprehensive with mostly complete data. Limitations included a relatively small sample size, which might have underpowered our study. Our work was also retrospective and depended mostly on paper charts; therefore, it is theoretically possible that some visits were missed. A few of our patients were preverbal at the end of their follow-up and did not have numerical visual acuity, and therefore were not included in computing final visual acuity.

Conclusion

Our study showed that PCG presented earlier and with a higher IOP than secondary glaucoma. These eyes were also operated on earlier. Both groups demonstrated good IOP control at the end of the follow-up period with PCG showing a better visual prognosis. Secondary glaucoma eyes required a higher number of medications at their final visit, reflecting the poorer IOP control of this group. When it came to surgeries, both groups underwent trabeculotomies most frequently. Prognostically, in the PCG group, an increased number of surgeries was associated with poor IOP control. In the secondary group, increased age at first surgery, unilateral disease, and multiple surgeries conferred a poor visual outcome.

Clinical Significance

Literature regarding the characteristics of pediatric glaucoma, especially in the Middle East, is scarce. Our study sheds light on the presentation of different types of pediatric glaucoma and their outcomes, namely IOP control and visual acuity.

Acknowledgments

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