Clinical and Experimental Vision and Eye Research (2018), 1, 9–13

ORIGINAL ARTICLE

Spectrum of presentation in primary congenital glaucoma and its relation to the early outcome

Sushmita Kaushik, Savleen Kaur, Indu Bala Dhiman, Adit Gupta, Srishti Raj, Surinder Singh Pandav

Department of Ophthalmology, Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, Punjab, India

Key words:

Outcome, presentation, primary congenital glaucoma

Address for correspondence:
Sushmita Kaushik,
Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, Punjab, India.
Phone: 91-172-2756111. Fax: 91-172-2747837.
E-mail: sushmita_kaushik@yahoo.com

Received: 05-07-2018;
Accepted 12-07-2018
doi: 10.15713/ins.clever.3

Abstract

Aim: This study aims to study the presentation pattern of primary congenital glaucoma (PCG) in Northern India and analyze the relationship to its outcome if any.

Methods: A total of 90 patients (157 eyes) with PCG presenting between January 2003 and December 2011, with at least 1-year follow-up after surgery were included in the study. Inclusion criteria were increased corneal diameter (>12.0 mm), intraocular pressure (IOP) >18 mmHg, and/or presence of Haab's striae with or without optic disc changes. Demographic data, whether the patient was self-reported or doctor referred, presenting IOP, corneal diameter, corneal clarity, and optic nerve damage where visualized, were recorded. Outcome of treatment was determined depending on IOP control and requirement of drugs. Differences in presenting feature between self-reported and doctor-referred patients, and association between presenting features and outcome was analyzed.

Results: Majority (67%) were self-reported. 102 eyes had hazy corneas; 45 eyes (28.7%) presented with corneal opacity. Doctor-referred patients presented earlier ($P \leq 0.001$), had significantly lower IOP ($P = 0.009$), and smaller corneal diameters ($P = 0.049$) than self-reported. Good outcome was correlated with lower IOP ($P = 0.005$) and smaller cornea ($P < 0.001$) at presentation. Corneal opacity at presentation was strongly correlated to poor outcome ($P < 0.001$). Optic disc cupping at presentation had no bearing on the final outcome.

Conclusions: Corneal involvement appears to occur early in this cohort of PCG. Corneal examination under torchlight by paramedical personnel, general physicians, and pediatricians might lead to an early referral before vision-threatening complications develop. However, early corneal involvement may indicate more severe disease and is likely to have a poor prognosis regardless of the time of referral.

Introduction

Primary congenital glaucoma (PCG) is a relatively uncommon condition but results in a lifetime of irreversible blindness if left untreated. There is a relatively narrow treatment window, which, if missed, is likely to lead to severe visual disability.

For any disease to be detected in time, it is important for the signs and symptoms to be recognized. Unlike glaucoma in adults, which is notoriously difficult to detect since there are no symptoms, glaucoma in children does present with symptoms and signs which can be detected by pediatricians and even parents, who are usually the first contacts of these children. PCG classically presents with a triad of photophobia, epiphora, and blepharospasm. Many children in India present with corneal edema initially, without buphthalmos or any of the classical signs.[1,2] Conversely, many children may have had symptoms for a considerable period of time, before presentation to an ophthalmologist simply because the disease was not thought of, hence, delaying diagnosis.

In India, there are few centers treating PCG and many children present too late for any meaningful treatment. Ours is the only tertiary care referral center treating PCG for five large states in

Northern India, with a combined population of approximately 84 million persons.[3] This gives us the opportunity to manage a large number of children with congenital glaucoma. We noticed that many of our children had severe corneal involvement very early in the disease, and this presentation seemed to be associated with poor outcome. Many infants presented with advanced disease when the parents noticed "something wrong." This study aimed to characterize the presentation patterns of PCG in this population, and if the outcome varied depending on how the child presents, and whether pediatricians referring children early mattered in the final outcome.

Materials and Methods

This was a retrospective review of patients with PCG presenting to a tertiary care center in North India and registered in the electronic database between January 2005 and December 2013, and completing 1-year follow-up after surgery. The study was approved by the Institute Ethics Committee (Vide Approval No 8906/PG-2Trg/2011/6279) and adhered to the tenets of the Declaration of Helsinki. Informed consent had been taken by the parents or legal guardians of all children.

All patients had to have been diagnosed PCG by any one of three glaucoma specialists (SSP, SK, and SR) based on characteristic clinical features including size of the globe, corneal features, intraocular pressure (IOP), and disc evaluation where possible with examination under anesthesia when required. All children identified as PCG were included for the analysis. The inclusion criteria were as follows:

1. Increased corneal diameter (>12.0 mm) along with raised IOP (>18 mmHg) and/or presence of Haab's striae;
2. Optic disc changes (where examination was possible);
3. History of epiphora, photophobia, and sudden corneal clouding was considered corroborating factors.

The following information was recorded at presentation for each case: Place of origin, birth history, family history, laterality, age of onset, and sex, whether the child was referred by a doctor or self-reported. The following ocular features at presentation were recorded: Visual acuity (whenever possible), IOP by applanation tonometry (Goldmann/Perkins), corneal diameter, and corneal clarity including the presence of corneal edema, corneal opacity or scarring, and disc evaluation for glaucomatous damage. Most of these features were recorded from findings noted at the first examination under anesthesia (inhalational anesthesia using sevoflurane) under the operating microscope. IOP was measured using the Perkins tonometer (Haag-Streit model, Clement Clark, Essex, England) as soon as the child was sedated to negate the effects of general anesthesia as far as possible. The horizontal corneal diameters were measured using Castroviejo's calipers. Corneal clarity was determined by observing iris details through the cornea under the microscope. Corneal status was evaluated as follows: Presence or absence of corneal edema, presence or absence of Haab's striae, and presence or absence of corneal scarring leading to corneal opacity. The severity of corneal edema was graded according to the visibility of the iris through the edematous cornea. Mild haze: Cornea hazy but iris details clearly visible; moderate Haze: Iris and pupil visible through the hazy cornea but no iris details visible; severe edema: Iris not visible through edematous cornea.

The number and type of surgical procedures and/or medications required to control IOP were recorded. IOP was regarded as satisfactory if <16 mmHg in patients examined under anesthesia, or <21 mmHg in children old enough to be examined with the slit lamp. The outcome was graded as good if the IOP was brought under control without drugs, satisfactory if up to two drugs was required to control IOP, and poor if the IOP was refractory to treatment needing three or more drugs for IOP control, or there was the development of hypotony or other sight-threatening complications.

The outcome was correlated to the factors listed above to see if the mode of presentation had any bearing on the outcome of treatment.

Statistical analysis

Statistical analysis was done using the IBM SPSS Statistics 19® program. Descriptive statistics were computed for all variables. Mann–Whitney *U*-test was used to analyze differences in presenting features such as IOP, corneal diameter, corneal clarity, and optic nerve damage where visualized between self-reported and doctor referral patients. Spearman's correlation was used to analyze association between outcome and presenting features. Linear regression was used to analyze if one could predict outcome from presenting signs.

Results

Data of 90 patients who fulfilled the inclusion criteria were analyzed [Table 1]. There were 34 female and 56 male patients who presented at a mean age of 4.36 ± 4.3 months and 4.5 ± 6.7 months, respectively (P = 0.91). The majority were self-referrals (67%) though boys tended to be referred by a doctor more often than girls (35% vs. 26%) though the difference was not significant. Self-reported patients presented significantly later than those referred by a doctor (5.64 ± 6.82 months vs.

Table 1: Patient demography

Patient parameter	Females (n=34)	Males (n=56)	Total (n=90)
Age at presentation			
Months (mean±SD)	4.36±4.3	4.5±6.7	4.5±5.9
Laterality			
Unilateral *n* (%)	9 (26.4)	14 (25)	23 (25.5)
Bilateral *n* (%)	25 (73.5)	42 (75)	67 (74.5)
Referral			
Self-reported *n* (%)	25 (73.5)	36 (64.2)	61 (67.7)
Doctor referred *n* (%)	9 (26.5)	20 (35.7)	29 (32.3)
Family history			
Present *n* (%)	3 (8.8)	4 (7.2)	7 (7.8)

1.9 ± 1.3 months, respectively; $P < 0.001$). Tearing and large appearing eyes were the most common cause of referral by a doctor, while corneal opacity in one or the other eyes was the most common reason for the referral in self-reported cases. 67 children (74%) presented with bilateral disease, which was similar in both boys and girls. Seven children had a history of a sibling or a parent with primary glaucoma, with equal incidence in boys and girls (four had siblings with PCG and three had a father with POAG). Most patients (86%) came from the states of Punjab (62%), Haryana (14%), and Himachal Pradesh (10%), reflecting the geographical proximity to our hospital.

157 eyes of these 90 children were analyzed for ocular findings and outcome. Presenting features are given in Table 2. Most eyes (104) presented with a hazy appearance of cornea with or without excessive tearing (66.2%). Six children had been advised sac massage for congenital dacryocystitis elsewhere. 45 eyes (28.7%) presented with corneal opacity noticed by the parents, and in another 34 eyes (21%), corneal opacity was discovered on EUA. Mean IOP at presentation was 18.9 ± 7.7 mmHg, and mean corneal diameter at presentation was 12.9 ± 1.9 mm. Corneal edema was detected in 43 (27.4%) eyes, Haab's striae in 73 (46.5%) eyes, and 79 (50.3%) eyes had a corneal opacity on EUA. There was no view of the disc in 21 eyes. Of the rest, 60% had cup-disc ratio <0.5, and 23% had advanced dice cupping (>0.8). The mean cup-disc ratio at presentation was 0.42 ± 0.28.

Table 2: Presenting ocular findings

Clinical feature	Total (*n*=157)
IOP at presentation	
Mean±SD	18.2±7.7 mmHg
Corneal diameter	
Mean±SD	12.9.±1.3 mm
Haab's striae	
Present *n* (%)	73 (46.5)
Corneal opacity	
Present *n* (%)	45 (28.7)
Optic disc status	
No view *n* (%)	21 (13.4)
C/D ratio<0.5 (*n* [% of discs viewed])	81 (59.5)
C/D ratio 0.6–0.8 (*n* [% of discs viewed])	23 (17)
C/D ratio>0.8 (*n* [% of discs viewed])	32 (23.5)

The pattern of referral of patients (self-reported and doctor-referred patients) was separately analyzed. Those children who were referred by a doctor presented earlier ($P \leq 0.001$) and had significantly lower IOP ($P = 0.009$) and had smaller corneal diameters ($P = 0.049$) and clearer corneas than those who reported by themselves [Table 3]. 74% of doctor-referred patients required only one surgical procedure compared to 58% of self-reported patients ($P = 0.03$). Poor outcome was observed in 31% of self-reported patients compared to 24% of doctor referred, though the difference did not reach statistical significance. Significantly, 64% of self-reported patients were under the care of some physician for non-ocular complaints or vaccinations but were not referred to an ophthalmologist.

Procedures required to control IOP are summarized in Table 4. 102 eyes (65%) could be controlled with one surgical procedure, 40 eyes (25.4%) required two procedures, 13 eyes (8.2%) underwent three surgeries, and two eyes required four surgeries to control the IOP. The most commonly performed primary procedure was trabeculotomy in approximately 2/3rd of eyes (104 eyes), followed by combined trabeculotomy with trabeculectomy in 28 eyes (18%), trabeculectomy with mitomycin C in 24 eyes (15%), and one child presented with a painful blind eye and underwent diode laser transscleral cyclophotocoagulation. 23 eyes needed an Ahmed glaucoma valve, which was the second procedure in nine eyes, third procedure in 12 eyes, and was implanted as the fourth procedure in two eyes. Two patients underwent optical penetrating keratoplasty after glaucoma surgery. Three patients developed a cataract after trabeculectomy and required intraocular lens implantation. Two patients had intractable glaucoma with poor visual prognosis and underwent diode CPC as the second procedure after trabeculectomy. The number of procedures required for IOP control correlated strongly with the IOP at presentation ($P = 0.003$).

111 eyes (70.7%) had satisfactory control of IOP with or without one or two drugs after surgery (good outcome), of which 58 eyes (37%) required no drugs. 46 eyes (29.3%) required more than two drugs after surgery for satisfactory IOP control. Good outcome was correlated with lower IOP at presentation ($P = 0.005$), lower age at presentation ($P = 0.034$), smaller corneal diameter at presentation ($P < 0.001$), and visibility

Table 3: Differences in presentation in self-reported patients and those referred by a doctor

Variable	Self-reported (*n*=50)	Doctor referred (*n*=107)	*P**	Total (*n*=157)
Age (months)				
Mean±SD	5.9±6.2	2.1±1.5	<0.001	4.5±5.9
IOP (mmHg)				
Mean±SD	19.4±7.7	15.9±7.2	0.009	18.2±7.7
Corneal diameter (mm)				
Mean±SD	13.1±1.4	12.7±0.9	0.049	12.9±1.3
Number under medical care for routine checkups (%)	32 (64)	107 (100)		

Table 4: Surgical procedures required to control IOP

Procedure	Primary procedure	Second procedure	Third procedure	Fourth procedure
Trabeculotomy	104 (66.2)	0	0	0
Trabeculotomy with trabeculectomy	28 (17.8)	0	0	0
Trabeculectomy with MMC	24 (15.3)	44 (80)	3 (20)	0
DLCP	1 (0.6)	2 (3.6)	0	0
Ahmed glaucoma valve	0	9 (16.4)	12 (80)	2 (100)
Total	157	55	15	2

IOP: Intraocular pressure

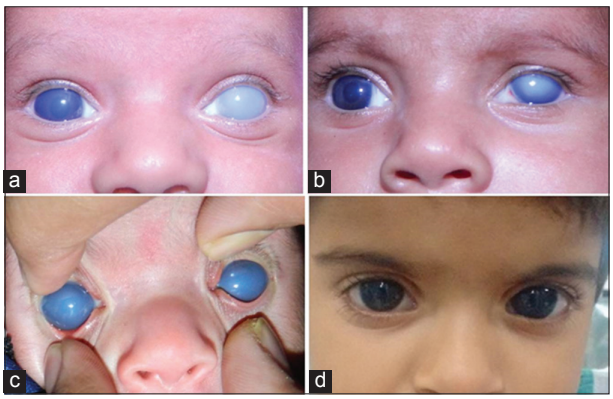

Figure 1: (a) A 7-day-old baby with PCG at presentation with acute hydrops in the left eye and corneal haze in the right eye, (b) at 6-month follow-up following combined trabeculotomy and trabeculectomy in both eyes. Note the clear cornea in the right eye and central scar in the left eye with peripheral clearing, (c) newborn baby (16 h) presenting with PCG with corneal haze in both eyes, (d) follow-up at 3 years following combined trabeculotomy and trabeculectomy in both eyes. Note the clear cornea in both eyes.

of Haab's striae during EUA (P = 0.024). The presence of corneal opacity at presentation was strongly correlated to poor outcome (P < 0.001) by linear regression analysis, lower IOP (P = 0.032), and absence of corneal opacity (P = 0.007) were predictive of good outcome(Figure 1). Optic disc cupping at presentation did not have any bearing on the final outcome. The mean follow-up was 22.67 ± 8.2 months (range 15–26 months).

Discussion

The incidence of PCG varies substantially in different ethnic groups from 1 in 1250 births in Slovakian Roms[4] to 1:20,000 in Scandinavian regions.[5] In the West, the average incidence is about 1 in 10,000 births,[6] but appears to be higher in Asians. In Saudi Arabia, it is reported to be 1:2500,[7] while Indian data from Andhra Pradesh reported an incidence of 1:3300.[8] Despite its infrequent incidence, PCG accounts for 7–20% of childhood blindness,[9-13] this disproportionate share of pediatric blindness may be because diagnosis is frequently delayed, resulting in an unnecessarily poor outcome despite appropriate treatment. Once the disease has advanced due to delayed diagnosis, little can be done in terms of visual rehabilitation of these children.[14]

PCG has been classically reported to present with tearing, photophobia, and blepharospasm,[12-15] but the scenario in the developing world may be very different. One study from Nigeria[16] reported seven of eight children presenting with corneal opacity. In another study from Africa, Bowman *et al.*[17] reported clear cornea at presentation in only 4 of the 47 eyes studied. In a large series from South India, Mandal *et al.*[1] reported clear corneas at presentation in only 10% of children with developmental glaucoma presenting before 6 months of age. Corneal edema persisted in >37% of children despite early surgery. In another report by the same group,[2] of 47 eyes with PCG operated within 1 month age, 46 presented with corneal edema, and one eye presented with corneal scarring. Even with such early treatment, one-third (32%) had persistent corneal edema after surgery.

In the BIG study, Papadoupoulous *et al.*[18] failed to find an association between IOP control and initial IOP, sex, ethnicity, time to surgery from diagnosis, corneal diameter, or the age of diagnosis. However, as they discuss it in their paper, the lower number of children (45) may have accounted for their result.

Among the 157 eyes of 90 children we studied, the average age of presentation was 4.5 months. Only 33.75% had clear corneas at presentation, and 45 eyes (29%) presented with corneal opacity. The presenting IOP was 18.9 mmHg and about 2/3rd of children had cup-disc ratios <0.5. This emphasizes that the IOP and disc findings considered "normal" in adults may not be valid for infants. In addition, since all these IOP measurements were taken under general anesthesia, they are likely to have been underestimated. Lower IOP, smaller corneal diameter, and corneal clarity at presentation were predictors for good outcome but not earlier age at presentation by itself. This highlights the importance of careful corneal examination in all infants being evaluated for PCG and also indicates that though some babies were referred early, if their cornea was severely affected, their prognosis was poor.

Nevertheless, we did observe that babies referred by doctors presented earlier, had lower IOP, better corneal features at presentation, and required lesser number of surgical procedures for IOP control compared to those who were self-reported. Waiting till parents note "something wrong" in the infant's eyes may tilt the balance toward poorer outcome than what could have been achieved by an early referral. An examination of the cornea under a hand light can be stressed on to pediatricians,

general practitioners, and also paramedical personnel who may be administering vaccinations, etc. This might lead to an early referral before vision-threatening complications develop. Recognizing signs of PCG such as large eyes, tearing, and hazy corneas will allow referral of at-risk infants at a time when good vision may be maintained, at least in those who have a reasonable prognosis of treatment.

It may be that delayed presentation may cause the cornea to worsen and thus compromise the outcome. However, we also noted that early corneal involvement may indicate more severe disease, and these infants are likely to have a poor prognosis. Recognizing the disease early would be the first steps toward early treatment and better outcomes. Long-term evaluation of the visual outcome of these infants correlated to the presentation would undoubtedly throw more light on how presentation patterns could be a guide to prognosticating the disease.

REFERENCES

1. Mandal AK, Bhatia PG, Bhaskar A, Nutheti R. Long-term surgical and visual outcomes in Indian children with developmental glaucoma operated on within 6 months of birth. Ophthalmology 2004;2:283-90.
2. Mandal AK, Gothwal VK, Bagga H, Nutheti R, Mansoori T. Outcome of surgery on infants younger than 1 month with congenital glaucoma. Ophthalmology 2003;110:1909-15.
3. Provisional Population Totals Paper 1 of 2011 India. Registrar General and Census Commissioner, India. New Delhi: Ministry of Home Affairs, Government of India; 2011.
4. Gencik A. Epidemiology and genetics of primary congenital glaucoma in Slovakia. Description of a form of primary congenital glaucoma in gypsies with autosomal-recessive inheritance and complete penetrance. Dev Ophthalmol 1989;16:76-115.
5. McGinnity FG, Page AB, Bryars JH. Primary congenital glaucoma: Twentyyears experience. Ir J Med Sci 1987;156:364-5.
6. Ho CL, Walton DS. Primary congenital glaucoma: 2004 update. J Pediatr Ophthalmol Strabismus 2004;41:271-88.
7. Bejjani BA, Stockton DW, Lewis RA, Tomey KF, Dueker DK, Jabak M, *et al*. Multiple CYP1B1 mutations and incomplete penetrance in an inbred population segregating primary congenital glaucoma suggest frequent de novo events and a dominant modifier locus. Hum Mol Genet 2000;9:367-74.
8. Dandona L, Williams JD, Williams BC, Rao GN. Population-based assessment of childhood blindness in southern India. Arch Ophthalmol 1998;116:545-6.
9. Gao DW, Kubota T, Sugino K, Sugai S, Inomata H. A statistical comparison study of glaucoma in the third affiliated hospital of China medical college and Kyushu university. Nippon Ganka Gakkai Zasshi 1989;93:458-65.
10. Kipp MA. Childhood glaucoma. Pediatr Clin North Am 2003;50:89-104.
11. Franks W, Taylor D. Congenital glaucoma--a preventable cause of blindness. Arch Dis Child 1989;64:649-50.
12. Dorairaj SK, Bandrakalli P, Shetty C, R V, Misquith D, Ritch R. Childhood blindness in a rural population of southern India: prevalence and etiology. Ophthalmic Epidemiol 2008;3:176-82.
13. Onakpoya OH, Adegbehingbe BO, Omotoye OJ, Adeoye AO. Causes of blindness in a special education school. West Afr J Med 2011;1:47-50.
14. Tanimoto SA, Brandt JD. Options in pediatric glaucoma after angle surgery has failed. Curr Opin Ophthalmol 2006;2:132-7.
15. Barsoum-Homsy M, Chevrette L. Incidence and prognosis of childhood glaucoma. A study of 63 cases. Ophthalmology 1986;10:1323-7.
16. Omoti AE, Uhumwangho OM. Problems of management of primary congenital glaucoma in Benin City, Nigeria. Niger Postgrad Med J 2007;4:310-3.
17. Bowman RJ, Dickerson M, Mwende J, Khaw PT. Outcomes of goniotomy for primary congenital glaucoma in East Africa. Ophthalmology 2011;2:236-40.
18. Papadopoulos M, Cable N, Rahi J, Khaw PT, BIG Eye Study Investigators. The British infantile and childhood glaucoma (BIG) eye study. Invest Ophthalmol Vis Sci 2007;48:4100-6.

How to cite this article: Kaushik S, Kaur S, Dhiman IB, Gupta A, Raj S, Pandav SS. Spectrum of presentation in primary congenital glaucoma and its relation to the early outcome. Cli Exp Vis Eye Res J 2018;1(1):9-13.