Primary Congenital Glaucoma: An Update

Arshi Singh, Kirti Singh
Department of Ophthalmology, Guru Nanak Eye Centre, New Delhi, India.

Abstract

Primary congenital glaucoma is a rare maldevelopment of the eye that affects children in the first few years of their lives. Blindness invariably occurs in untreated individuals. Early diagnosis by detailed examination under anaesthesia followed by prompt treatment is necessary for favourable visual outcomes. Surgery is the primary treatment modality due to limited role of medical management. Visual rehabilitation with management of refractive errors and amblyopia is key for long term visual success. This article gives an overview of the epidemiology, genetics, diagnosis and treatment of this devastating disease.

Keywords: Primary Congenital Glaucoma (PCG), Childhood Glaucoma, Trabeculodysgenesis

Introduction

Primary congenital glaucoma occurs due to abnormal development of trabecular meshwork and anterior chamber angle leading to impaired aqueous outflow. The terminology has replaced the older term Buphthalmos (Greek: bous = ox; ophthalmos = eye) which is now restricted to primary congenital glaucoma occurring before 3 years of age with resultant increased growth in eye ball. The dismal disease consequences emphasised by Anderson’s comment “Future of hydrophthalmia patients is dark and one seeks in vain for a best operation in treatment” have changed over the last few decades to more promising outcomes. This review traces the improved understanding and treatment evolution of this condition.

Historical Trail

Although abnormal large eyeballs in children were recognized by Hippocrates (4th century BC) and Celsus (1st century AD), it was only in late nineteenth century that von Hippel and Parsons linked disease pathology to malformation of anterior chamber angle.

The first successful surgery ‘goniotomy’ by Otto Barkan, in 1938 was modification of de Vincentis goniotomy, name derived from Greek gonio (angle), tomein (cut) by designing a glass contact lens to visualize and knife to cut trabecular tissue. Two decades later ‘ab externo trabeculectomy’ was simultaneously and independently performed by Burian with metal probe and Redmond Smith with nylon filament, which ushered in the era of Schlemm’s canal surgery.

Classification

Primary congenital glaucoma was classified according to age or pathology.

1. According to age of onset
   • Congenital glaucoma - disease presence at / before birth
   • Infantile glaucoma- birth until 3 years
   • Juvenile glaucoma- 3 years to teenage

2. Anatomical classification (Hoskins–Shaffer–Hetherington) 5
   • Isolated trabeculodysgenesis as flat iris insertion or concave (wrap-around) insertion
   • Irido-trabeculodysgenesis with anterior stromal defects (hypo/hyperplasia), anomalous iris vessels (persistence of tunica vasculosa lentis /anomalous vessels) or structural anomalies (holes, colobomata, aniridia)
   • Corneotrabeculodysgenesis - peripheral (Axenfeld’s anomaly), mid-peripheral (Rieger’s anomaly), central (Peter’s anomaly)
   • Corneal size (micro/ macrocornea)

3. Congenital Glaucoma Research Network (CGRN) - current classification

Combines disease severity with associated ocular anomalies

a. Primary glaucoma:
   • PCG: glaucoma at birth to 1-year, neonatal (0–1 month)
   • Infantile glaucoma: 1–3 years
   • Juvenile open angle glaucoma: 3 to 16 years
   • Spontaneously arrested cases: normal IOP & signs of PCG

b. Secondary glaucoma associated with:
   • Non-acquired ocular anomalies (anterior segment dysgenesis)
   • Systemic disease or syndrome (Sturge–Weber)
   • Post congenital cataract surgery (aphakia/ pseudophakia)
   • Acquired conditions (Steroid-induced, traumatic, uveitic)

Epidemiology

Prevalence has racial connects varying from 1 in 10,000/68,254 live births. (Caucasians) 8-9 to 1 in 2,500 (high rate of consanguinity eg. Slovakian Gypsies and Middle East) 2,10 to 1 in 3,300 (India). Consanguinity promotes founder effect or frequent mutations of a key mutation in an ancestor with reported 45–80% consanguinity in PCG cohorts. 12,13

Age of presentation is also linked to race, with early disease at 3-6 months in Asians /Arabians to 11-12 months in Caucasians. 14,15 British Infantile glaucoma study (BIG) reports earlier age of presentation in children with Asian background (50% present before 3 months) compared to Caucasian peers (52% by 6 months). Disease phenotype is more severe in developing countries, with almost 2/3rd PCG children in India presenting with blindness and most reporting late, after 6 months. 17

Slight male predominance (65%) has sometimes been noted for both Western and Asian cohorts. 3,10 Bilateral disease is the rule (70-85%). Since asymmetric presentation occurs and fellow “apparently normal, currently disease free” eye develops subclinical disease, it is imperative that children of unilateral PCG have lifetime screening.
Genetics
Occurrence is sporadic with familial inheritance in 10–40% cases (autosomal recessive with incomplete or variable penetrance). Genetic loci identified are GLC3A, 3B, 3C and 3D. GLC3A loci (chromosome 2p21): Around 120 mutations have been described with mutations in CYP1B1 gene, encoding cytochrome P450 enzyme being commonest at 42%. Gene effect has been traced to monoxygenase enzyme in endogenous steroid metabolism with Tyrosinase deficiency concurrence resulting in severe phenotype.

GLC3B loci (chromosome 1p36): Implicated gene is CDT6/ANGPTL coding for extracellular matrix organization (ECM) and formation

GLC3C loci (chromosome 14q24): gene LTBP2

GLC3D loci (chromosome 14q24): Gene implicated is latent transforming growth factor β binding protein responsible for ECM organization and formation

TIGR/MYOC gene (chromosome 1q24.3--q25.2): linked to juvenile onset glaucoma, autosomal dominant inheritance.

Other associated genes: COL1A1 (17q21.33), FOXC1 (6p25.3), ANGPTL (8q23.1), TEK (9p21.2).

Genetic unravelling introduces molecular screening as the preferred prevention tool in asymptomatic individuals with a high risk of disease, and for prenatal diagnosis. It is already being done for Slovak gypsies.

Clinical Manifestations
Classical triad remains blepharospasm, epiphora and photophobia with large eyeball with hazy corneas emerging to be more common in Indian subcontinent. Corneal: Corneal enlargement implies disease onset prior to 3 years. Corneal diameter of >11 mm (newborn), >12 mm (infant) and >13 mm (any age) is suspicious (Table 1).

Table 1: Normal milestones with age

| Age            | Normal (mm) | Suspicious |
|----------------|-------------|------------|
| Birth - 6 months | 9.5-11.5    | >12        |
| 1-2 yr         | 10-12       | >12.5      |
| >2 yr          | < 12        | > 13       |
| IOP (mmHg)     |             |            |
| Birth - 1 year | 10-12 + 3.7 |            |
| 1-2 years      | 12          |            |
| 3-5            | 13.6        |            |
| 7-9            | 14.3        |            |
| Axial length (mm) |             |            |
| New-born       | < 18        |            |
| 10-75 days     | 17.22-18.77 |            |
| 10-36 months   | 20.14-22.0  |            |
| 4-10 years     | 22.78-23.12 |            |

Haab’s striae due to breaks in Descemet’s membrane are hallmark of disease. Typically horizontal and linear in central cornea or parallel /curvilinear to limbus in peripheral cornea, they need to be differentiated from post forces assisted birth trauma Descemet tears, the latter being aligned vertically.

Corneal edema progress is from epithelial to stromal edema and scarring in case of persistently raised pressures.

Intra-Ocular Pressure And Its Measurement
Intraocular pressure (IOP) measurement depends on anaesthesia stage/agent, corneal thickness, corneal edema and corneal biomechanics. Scleral / corneal stretch with reduced corneal hysteresis may mask the IOP rise.

Effect of corneal hysteresis (CH) and corneal resistance factor (CRF) on IOP is significant, with both indices being reduced in PCG. Measured by Reichert’s Ocular Response Analyzer (ORA), corneal compensated IOP is independent of corneal thickness.

Cornea is thicker in diseased eyes, with same being confirmed by studies excluding corneal edema situations. Few authors however report thinner corneas. Poor corneal clarity makes optical tools like IOL Master under-estimate CCT significantly (almost 40μm) compared to ultrasound pachymetry.

Optic Disc Dimensions
Disc excavation of > 0.1 C: D ratio in children younger than 1 yr should be regarded with caution and > 0.3 most certainly investigated for glaucoma. Elasticity of scleral canal sometimes partly reverse this cupping.

Examination Under Anaesthesia (EUA)
Ophthalmic examination under sedation (intravenous or mask anaesthesia) suffices for diagnosis, followed by general anaesthesia for definitive surgery.

Protocol for EUA

- Intraocular pressure (IOP): All anaesthetic agents except ketamine, succinylcholine, and cyclopropane cause rapid lowering of IOP (30 % reduction). Excitement, intubation and induction artificially elevate IOP. Protocol mandates IOP measurement immediately post intubation. Perkins hand-held applanation tonometer or Tonopen for edematous cornea, are the preferred measuring tools.

- Corneal diameter - white to white dimensions are measured in both vertical and horizontal diameters. Corneal thickness measurement.

- Gonioscopy is done with Koepppe lens (14–16 mm diameter) combined with hand-held slit-lamp or operating room microscope. Iris insertion is often high (wrap around), obscuring trabecular meshwork. Iris contour is usually flat, rarely concave. Vascular loops from major arterial circle, “Loch Ness Monster phenomenon” maybe seen. Rarely fine, fluffy tissue obscures peripheral iris called “Lister’s morning mist”. Alternatively, a four mirror Zeiss indirect goniolens can also be used during EUA or on slit lamp examination for older children. In addition ,we can
photograph the angle for documentation using the RETCAM® wide-angle lens.

- **Ophthalmoscopy:** Optic disc cup is usually central, round with steep-walls. Cupping enlarges circumferentially due to stretching of scleral canal, in variance with polar notching of adult glaucoma.³
- **Refraction:** Axial myopia is a result of uncontrolled IOP. Progressive myopia or myopic shift presages PCG and glaucoma secondary to aphakia.

**Surgical Treatment**

Surgical treatment is the mainstay of therapy. Medical therapy serves as a stop gap, an adjunct post-surgery or in interval between repeat surgery to allow time for visual maturation.

Beta-blockers are first line drugs, resulting in 30% reduction in IOP.⁴ Systemic side effects are minimized by using 0.25% dose or punctal occlusion. Both systemic and topical carbonic anhydrase inhibitors (CAIs) are effective, with topical Dorzolamide being the 2nd option.⁴⁰ Oral acetazolamide is used with caution due to its systemic side effects of respiratory depression and fatigue⁴⁷,⁴⁸ Prostaglandin analogues are the last resort, majority of children being non-responders.⁴⁹ Irreversible iris pigmentation and eyelash elongation side effects require counselling, especially in unilateral PCG. Sustained release implants have been developed.⁵⁰

**Surgical Treatment**

Surgery is the mainstay with options dictated by corneal clarity and disease severity. Surgical interventions are of two types:

- **Ab-interno surgeries:** Goniotomy, circumferential Schlemm’s canal surgery
- **Ab externo surgeries:** Trabeculotomy with or without Mitomycin C, trabeculotomy, combined trabeculotomy with trabeculotomy (CTT) or use of Glaucome drainage devices. CTT is the surgery preferred for severe disease and in eyes presenting with cloudy cornea.⁵¹ Due to this aspect it remains the most often performed surgery for PCG in Indian subcontinent at 80%. ¹⁴ However the recent Cochrane meta-analysis suggests that there may be little to no difference between CTT and routine conventional trabeculotomy, or between viscotrabeculotomy and routine conventional trabeculotomy.⁵² It stated that 360-degree circumferential trabeculotomy may show greater surgical success than conventional trabeculotomy.⁵²

**Goniotomy**

The procedure requires a clear cornea for proper visualization of angle structures. Tissue obstructing trabecular meshwork is incised by Barraquer knife/ Worst knife/ long 25 or 30 gauge needle, under direct visualization of Swan-Jacob gonioscopic lens in a viscoelastic formed chamber. Entry is from temporal clear cornea and nasal 3-4 clock hours are treated.⁵³ Globe rotation manoeuvre permit excision of 5-6 clock-hours of meshwork⁵⁴,⁵⁵. Trabecular meshwork is incised circumferentially laying bare a white line, followed by falling back of iris. A single goniotomy is effective in controlling pressures in almost 75% cases⁵⁶, multiple goniotomies increase the success rate to 93%.⁵⁷,⁵⁸

Modifications of the procedure are: twin site approach for wider coverage, Kahook dual blade use for more controlled incision and endoscopic goniotomy.⁵⁹-⁶². Goniotomy has the advantage of short operating time, conjunctiva-sparing nature, with low incidence of complications.⁵³,⁵⁷. Hyphema is a common complication, but it resolves with time.

**Sclemm’s Canal Surgery**

- **Trabeculotomy ab-externo (Burian and Smith)⁶³:** Similar to traditional trabeculectomy until raising of superficial scleral flap. Schlemm’s canal (SC) is subsequently de-roofed by incising at blue-gray zone (anterior) junction with white scleral zone (posterior), followed by threading a side defined trabeculotomy (metal probe) into open ends of SC. Rotation of the probe towards anterior chamber collapses trabeculum, ruptures inner wall of SC thereby re-establishing communication between anterior chamber and Schlemm’s canal. The procedure is repeated on other side with another trabeculotomy designed for that side, covering 120–180° of trabeculum. Both the scleral and conjunctival flap are then sutured. Success rates are high (90%).⁶⁴-⁶⁶ however the procedure is hampered by difficulty in identifying Sclemm’s canal in presence of limbus distorted by stretching. Hyphema, false passage creation, Descemet’s detachment, cycloidalysis, vitreous loss, vitreous haemorrhage, lens damage and choroidal detachment are other complications.
- **Ab externo Circumferential 360° trabeculotomy**

First performed by Beck and Lynch in 1995, using a 6/0 polypropylene suture passed in a purse string manner to create a 360-degree incision in inner wall of Schlemm’s canal.⁶⁷ Sustained IOP control with a single session, with success rates of 87- 93% over long term follow-up are reported.⁶⁸-⁷⁰ Few unacceptable complications being creation of false passage due to suture misdirection, subretinal and suprachoroidal damage iris tear and prolonged hypotony.⁶⁹,⁷¹

- **Illuminated micro-catheter assisted trabeculotomy (IMCT)** replaced suture guided trabeculotomy in an attempt to reduce complications. Fibreoptic devices used are: Glaucolight (DORC International, Zuidland, The Netherlands) or iTrack microcatheter (Ellex, Adelaide, SA)⁷². The iTrack microcatheter (200 μm diameter shaft, 70μm central lumen permitting viscoelastic injection) differs from Glaucolight microcatheter (smaller diameter of 150
μm sans lumen). Both devices incorporate an optical fibre illuminating the tip, permitting continuous visualization. After 360 degree catheterization, catheter is retrieved from other cut end of Schlemm’s canal and two ends of catheter are pulled like a purse string, resulting in 360° rupture of inner wall of Schlemm’s canal. Success rates range from 80-87%, 72,73 Complications reported are hyphaema in 100%, canal malformation restricting catheterization in 7-20% and cataract. 72,74,75

Trabeculectomy With Mitomycin-C
A tested surgery with long term success rates ranging from 60-90 %, 76,77 adjunctive anti-metabolites improve success. 78,79 Mitomycin-C is used in doses ranging from 0.2 - 0.4 mg/ml for durations of 2 - 3 minutes. 80 Postoperative complications like prolonged hypotony, scleral and conjunctival fragility and endophthalmitis are known consequences of MGC use. 81 The most problematic aspect of creation of bleb for life with subsequent tear film abnormalities, corneal astigmatism and bleb related infections. Propensity to eye rubbing and trauma often results in high rates of bleb related endophthalmitis in children (7-14%). 78-80,82

Combined trabeculotomy with trabeculectomy (CTT)
This surgery combines conventional trabeculectomy with Schlemm’s canal exploration and rupture of its inner walls by Harm’s trabeculotome. This is followed by excision of deeper trabecular block and suturing of superficial scleral flap and conjunctival flap.

Combined trabeculotomy and trabeculectomy with or without MMC is the most commonly procedure for PCG eyes in Asia, with figures as high as 80% in Indian scenario. 14,85 Success of the procedure ranges from 85 % at 1 year declining to 75 -77 % over a 2-3 year follow up. 31,84 A large series of 624 eyes with a 3 year follow up and 299 with over 8 year follow up report success rates of 77 and 63% respectively. 84,85 The longest reported follow up till date of 21 years from India has documented 6% compete success with 63% qualified success. 86

Glaucoma Drainage Devices (GDD)
Glaucoma drainage implants (GDD) come to rescue in situations of multiple failed angle and or limbal surgeries. 87 Bleb of GDD being posterior to limbus makes it less susceptible to endophthalmitis. Tube implants currently used in pediatric glaucoma are Baerveldt and Ahmed tube shunts. For smaller sized eyes, smaller area models of FP 8 Ahmed valve (96 mm2) compared to FP7 (184 mm2) and 250 mm2 size Baerveldt compared to 350 mm2 (adult) version are recommended. 88 Keeping in mind anticipated growth of child’s eye with high incidence of tube retraction, some recommend adult size implants if it can fit the paediatric eye.19

Efficacy of tube shunts in PCG has been reported to be high from 87-90% at 1 year 87-82 however survival declines over time, from 80-97% during first year to 58-66 % by 2-4 years and 20-40% by 5 -10 years. 87,89-93 Comparative studies score GDD to perform better than trabeculectomy with success of 87 to 53% (at 1 and 6 year) compared to 36 and 19% with trabeculectomy. 93,94 The same group reported more postoperative complications with GDD use in children, especially tube repositioning.

Long term complications are otherwise high with reported pupil abnormalities (16%), cataract (20% of phakic eyes), corneal touch, corneal decompensation (10%). 89 Hypertensive phase post tube shunts is less frequently seen in children 87,93 and is controlled by prophylactic use of aqueous suppressants. 88 Conditions peculiar to the child’s eye like eye rubbing, growth and elasticity result in specific complications namely corneal decompensation, tube erosion /extrusion and tube retraction. 82,88 Elastoc recoil of sclera after normalization of IOP can cause tube rotation leading to corneal contact. Growth of eyeball carries the potential risk of tube retraction. Treatment of latter is done with tube extenders or by tube-in-tube technique (threading new tube within existing tube lumen) 94

Deep Sclerectomy
Utility of non-penetrating deep sclerectomy is doubtful given that obstruction to aqueous humour flow is internal, with only few studies supporting its success in PCG eyes. 95,96

Cyclophotocoagulation
Cyclophotocoagulation by transscleral Nd:YAG, transscleral diode, endoscopic diode, or micropulse trans-scleral diode are reserved for eyes with guarded visual prognosis, has a success rate ranging from 28 - 79% 97-99 Transscleral cyclophotocoagulation diode (TSCPC) is safe and effective, however efficacy is often transient and several sessions are required. Lens opacification requiring cataract surgery is common in phakic eyes (40%). 100

Prognosis And Complications
Visual gain in children depends on the degree of corneal scarring, astigmatism, anisometropic amblyopia, extent of glaucomatous damage and sequel like cataract or strabismus. Timely surgery with amblyopia therapy can result in good vision and a large series of 624 eyes from India reports 42% children gaining near normal vision. 84 Functional gain of vision occurs in 50-80% patients when IOP, refractive error and amblyopia are managed adequately. 58,69,101 A long follow up of 28 years in 121 children 102,103 documented minimal visual impairment in 42 % and low vision in 42 %. 86

Axial myopia is common (50 % and more), with younger age of surgery related to worse retinal parameters. 100 Cataract and strabismus often occur after successful PCG surgery. Cataract surgery requirement is reported for 22% within 8 years and strabismus for 38% over 5 years increasing to 50% over 10 years. 102-104 Risk factor for occurrence of cataract are number of anti-glaucomatous surgeries and tube shunts. Performing strabismus or cataract surgery in filtered eyes can have an adverse effect on bleb longevity, due to liberation
of inflammatory cytokines. Performing cataract surgery can also result in refractive surprise primarily due to greater myopic shift, subsequent to increased responsiveness to IOP fluctuation. Visual acuity improvement post-surgery is gratifying, however these children need to be monitored for lens subluxation, capsular phimosis and endophthalmitis. Visual sequel to PCG surgery have clinical implications in visual prognosis and counselling of parents. Consent for probable need of strabismus surgery, cataract surgery, amblyopia therapy and low visual aids should be taken from the parents prior to performing surgery. Management of residual vision with and lifelong follow-up and low vision aids is integral to enable these children to retain functionality.

**Conclusion**

Early diagnosis, appropriate surgical management before irreversible damage ensues can result in functional visual gain to most of the children of primary congenital glaucoma. Choice of surgery depends on the severity of glaucoma- goniotomy being preferred in milder disease and clearer corneas, CTT or assisted goniotomy in severe PCG. We reserve use of drainage implants or cyclodestruction for cases with surgical failure. Medication can help pre- and post-operatively for IOP spikes. Genetic counselling, molecular diagnosis, possibly antenatal and reversing the trend of consanguineous marriage in certain populations are the means to reduce this devastating childhood blindness.

**References**

1. Allingham RR, Damji K, Freeman S, Moroi S, Shafranov G. Congenital glaucomas and developmental glaucomas with associated anomalies. In: Allingham RR, Damji KF, Freedman S, Moroi AE, Rhee DJ, editors. Shields Textbook of Glaucoma. 5 ed. Philadelphia, PA: Lippincott Williams &Wilkins; 2005. p. 235–271.
2. Badawi AH, Al-Muhaylib A, Al Owaifeer AM, Al-Essa RS, Al-Shahwan SA. Primary congenital glaucoma: An updated review. Saudi J Ophthalmol. 2019; 33(4): 382–388.
3. Mandal AK and Chakrabarti D. Update on congenital glaucoma. Indian J Ophthalmol. 2011 Jan; 59(Suppl1): S148–S157.
4. Barkan O. Technique of goniotomy. Arch Ophthalmol. 1938;19:217–221.
5. Hoskins H.D., Jr., Shaffer R.N., Hetherington J. Anatomical classification of the developmental glaucomas. Arch Ophthalmol. 1984; 102:1331–1336.
6. Beck A, Chang TC, Freedman S. Definition, classification, differential diagnosis. In: Weinreb RN, Grajewski A, Papadopoulos M, Grigg J, Freedman S, editors. Childhood Glaucoma. Consensus series 9. Amsterdam: Kugler Publications; 2013. p. 3-10.
7. Hoguet A, Grajewski A, Hodapp E, Chang TC. A retrospective survey of childhood glaucoma prevalence according to Childhood Glaucoma Research Network classification. Indian J Ophthalmol. 2016;64:118-23.
8. Francois J. Congenital glaucoma and its inheritance. Ophthalmologica. 1972;181:61–73.
9. Tancelik N, Atalay E, Bolukbasi S, Capar O, Ozkok A. Demographic features of subjects with congenital glaucoma. Indian J Ophthalmol. 2014;62(5):565–569.
10. Genieck 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.
11. Dandona L, Williams BC, Rao GN. Population-based assessment of childhood blindness in Southern India. Arch Ophthalmol. 1998;116:545–6.
12. Helmy H Combined trabeculotomy-trabeculectomy versus Ahmed valve implantation for refractory primary congenital glaucoma in Egyptian patients: a long-term follow-up. Electronic Physician 2016, 8 (2): 1884-1891.
13. Genieck A, Genicekova A, Ferak V. Population genetical aspects of primary congenital glaucoma. Incidence, prevalence, gene frequency, and age of onset. Hum Genet. 1982; 61:193–7.
14. Senthil S, Badakere S, Ganesh J, Krishnamurthy R, Dikshit S, Choudhari N, Garudadri C, Mandal AK. Profile of childhood glaucoma at a tertiary center in South India. Indian J Ophthalmol 2019;67:358-65.
15. Fung DS, Roensch MA, Kooner KS, Cavanagh HD, Whitson JT. Epidemiology and characteristics of childhood glaucoma: results from the Dallas Glaucoma Registry. Clin Ophthalmol. 2013;7:1739–1746.
16. 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.
17. 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. Clinical and Exp Vision and Eye Research J 2018, 1(1): 9-13.
18. Bayoumi NHL. Fellow Eye in Unilateral Primary Congenital Glaucoma J Curr Glaucoma Pract. 2017 Jan-Apr; 11(1): 28–30.
19. Mocan MC, Mehta AA, Aref AA. Update in Genetics and Surgical Management of Primary Congenital Glaucoma. Turk J Ophthalmol. 2019; 49:347-355.
20. Kaur K, Mandal A.K., Chakrabari S. Primary congenital glaucoma and the involvement of CYP1B1. MEAOJ. 2011; 18:7–16.
21. Panicker SG, Reddy ABM, Mandal AK, Niyaz Ahmed N, Nagarajaram HA, Hasnain SE et al. Identification of Novel Mutations Causing Familial Primary Congenital Glaucoma in Indian Pedigrees Investigative Ophthalmology & Visual Science 2002, 43(5): 1358-1366.
22. Choulier L and Nadifi S. Analysis of CYP1B1 Gene Mutations in Patients with Primary Congenital Glaucoma. J Pediatr Genet. 2017 Dec; 6(4): 205-214.
23. The Human Gene Mutation Database. [Internet]. [place unknown: publisher unknown]; 2007. Available from: http://www.hgmd.org.
24. Sarfarazi M, Akarsu AN, Hossain A. Assignment of a locus (GLC3A) for primary congenital glaucoma (buphthalmos) to 2p21 and evidence for genetic heterogeneity. Genomics. 1995, 30:171–77.
25. Stollow I, Akarsu AN, Sarfarazi M. Identification of three different truncating mutations in cytochrome P450B1 (CYP1B1) as the principal cause of primary congenital glaucoma (Buphthalmos) in families linked to the GLC3A locus on chromosome 2p21. Hum Mol Genet 1997, 6 (04):641–647.
26. Ling C, Zhang D, Zhang J, Sun H, Du Q, Li X. Updates on the molecular genetics of primary congenital glaucoma (Review). Exp Ther Med. 2020;20(2):968-977.
27. Sihota R, Tuli D, Dada T, Gupta V, Sachdeva M M. Distribution and determinants of intraocular pressure in a normal pediatric population. J Pediatr Ophthalmol Strabismus. 2006, 43:14–18.
28. Zareef A, Razegheinjad MR and Salouit R. Corneal Biomechanical Properties and Thickness in Primary Congenital Glaucoma and Normal Eyes: A Comparative Study. Med Hypothesis Discov Innov Ophthalmol. 2018 summer, 7(2): 68–72.
29. Dascalescu D, Corbu C, Vasile P, Iancu R, Cristea M, Ionescu C, et al. The importance of assessing corneal biomechanical properties in glaucoma patients care - a review. Rom J Ophthalmol. 2018;67(4):219–25.
30. Kirwan C, O’Keefe M, Lanigan B. Corneal hysteresis and intraocular pressure measurement in children using the Reichert ocular response analyzer. Am J Ophthalmol. 2006; 142(6):990-2.
31. Peruchó-González P, Martínez de la Casa JM, Morales-Fernández L, Bañeros-Rojas P, Saenz-Francés F, García-Feijóo J. Intraocular pressure and biomechanical corneal properties measured by ocular response analyser in patients with primary congenital glaucoma. Acta Ophthalmol. 2016, 94(5):293-7.

32. Doornenbal A, Yazdani S, Ansari S, Pakravan M, Motevasseli T, Hosseini B, Yasser M. Corneal profile in primary congenital glaucoma. Acta Ophthalmol. 2017; 95(7):e575-e581.

33. Kaushik S, Pandav SS, Banger A, Aggarwal K, Gupta A. Relationship between corneal biomechanical properties, central corneal thickness, and intraocular pressure across the spectrum of glaucoma. Am J Ophthalmol. 2012, 153(5):840-9 e2.

34. Razeghinejad MR, Tajbakhsh Z, and Nowroozzadeh MH. Agreement in central corneal thickness measurements between optical and ultrasonopachymeters in patients with primary congenital glaucoma. Eye (Lond). 2017, 31(9): 1382.

35. Lopes JE, Wilson RR, Alvim HS, Shields CL, Shields JA, Calhoun J et al. Central corneal thickness in pediatric glaucoma. J Pediatr Ophthalmol Strabismus 2007, 44 (2):112-7.

36. F. Aptel, P-L. Cornut, C. Burillon, P. Denis; Corneal Thickness in Congenital Glaucoma. Invest. Ophthalmol. Vis. Sci. 2005;46(13):4872.

37. Henriques MJ, Vessani, R M, Costa Reis FA, Vincenve de Almeida G, Betinjane AJ, Susanna Jr R. Corneal Thickness in Congenital Glaucoma Journal of Glaucoma: 2004, 13(3):185-189.

38. Wygnanski-Jaffe T, Barelou QT. Central Corneal thickness in Congenital Glaucoma Cornea: 2006, 25(8): 923-925.

39. Zhou G. The C/D ratio in normal newborns. Zhonghua Yan Ke Za Zhi 1993, 29(2):105-7.

40. Erkki H, Laatikainen L. Characteristics of optic disc in healthy school children. Acta Ophthalmol (Copenh) 1979; 57: 914–921.

41. Quigley H A. The pathogenesis of reversible cupping in congenital glaucoma. J AAPOS. 2005; 9(4):321–325.

42. Dietlein TS, Jacobi PC, Krieglstein GK. Assessment of diagnostic criteria in management of infantile glaucoma. An analysis of tonometry, optic disc cup, corneal diameter and axial length. Int Ophthalmol. 1996;20:21–27.

43. Ausinsch B., Munson E.S., Levy N.S. Intraocular pressures in school children. Acta Ophthalmol 2016, 94(5):321-325.

44. Levy J, Lifshitz T, Rosen S, Tessler Z, Biedner BZ. Is the tono-pen tonometry, optic disc cup, corneal diameter and axial length. Int Ophthalmol. 1996, 20(1):117-123.

45. Catalano RA, King RA, Calhoun JH, Sargent RA. One versus two simultaneous goniotomies as the initial surgical procedure for primary infantile glaucoma. J Pediatr Ophthalmol Strabismus. 1989;26:9-13.52.

46. Harvey MM, Schmitz JW. Use of ab interno Kahoock Dual Blade trabeculotomy for treatment of primary congenital glaucoma. Eur J Ophthalmol. 2018;14: 1120672118805873.

47. Kulkarni SV, Damji KF, Fournier AV, Pan I, Hodge WG. Endoscopic goniotomy: early clinical experience in congenital glaucoma. J Glaucoma. 2010; 19:264-269.

48. Bayraktar S, Koseoglu T. Endoscopic goniotomy with anterior chamber maintainer: surgical technique and 1-year results. Ophthalmic Surg Lasers. 2001;32(6):496–502.

49. Smith R. A new technique for opening the canal of Schlemm. Preliminary report. Br J Ophthalmol. 1960; 44:370–373.

50. Mandal AK, Netland PA. 1st ed. Amsterdam: Elsevier; 2006. Primary Congenital Glaucoma. The pediatric glaucomas.

51. Fulcher T, Chan J, Lianian B, Bowell R, O'Keefe M. Long-term follow-up of primary trabeculotomy for infantile glaucoma. Br J Ophthalmol. 1996, 80: 499–502.

52. Zhang X, Tu S, Fan Q, Peng S, Yu M, Ge J. Long-term surgical outcomes of primary congenital glaucoma in China. Clinics (Sao Paulo) 2009, 64 (6):543–551.

53. Beck AD, Lynch MG. 360 degrees trabeculotomy for primary congenital Glaucoma. Arch Ophthalmol 1995, 113(9): 1200–12.

54. Lim ME, Neely DE, Wang J, Haider KM, Smith HA, Plager DA. Comparison of 360-degree versus traditional trabeculotomy in pediatric glaucoma. J AAPOS 2015; 19:145-149.

55. Mendicino ME, Lynch MG, Dragk A, Beck AD, Harbin T, Pollard Z, Vela MA, Lynch MJ. Long-term surgical and visual outcomes in primary congenital glaucoma: 360 degrees trabeculotomy versus goniotomy. Journal of AAPOS. 2000, 4:205-210.

56. Neustein RF, Beck AD. Circumferential Trabeculotomy versus Conventional Angle Surgery: Comparing Long-term Surgical Success and Clinical Outcomes in Children with Primary Congenital Glaucoma. Am J Ophthalmol. 2017, 183:17-24.

57. Neely DE. False passage: a complication of 360 degrees suture trabeculotomy. J AAPOS. 2005, 9 (4):396–397.

58. Shakrawal J, Bali S, Sidhu T, Verma S, Sihota R, Dada T. Randomized trial on illuminated-microcatheter circumferential trabeculotomy versus conventional trabeculotomy in congenital glaucoma. Am J Ophthalmol. 2017,180:158–64.

59. Temkar S, Gupta S, Sihota R, Sharma R, Angmo D, Pujari A et al. Illuminated microcatheter circumferential trabeculotomy versus combined trabeculotomy trabeculectomy for primary congenital glaucoma: a randomized controlled trial. Am J Ophthalmol 2015;159 (3):490-7.

60. El Sayed Y and Gawdat G. Microcatheter-assisted trabeculotomy versus two-site trabeculotomy with the rigid probe trabeculotomy in primary congenital glaucoma. Journal of Glaucoma: 2018, 27(4): 371-376.

61. Celea C, Dragoslovaneau S, Pop M, Celea C. Comparison of 360-degree Circumferential Trabeculotomy and Conventional Trabeculotomy in Primary Pediatric Glaucoma Surgery: Part 1. Pediatr Ophthalmol Strabismus 2016; 53(6):357-64.

62. Mandal AK, Prasad K, Naduvilath TJ. Surgical results and (congenital glaucoma) Surv Ophthalmol. 1983; 28:1–19.

63. Sharaawy T, Bhartiya S. Surgical management of glaucoma: evolving paradigms. Indian J Ophthalmol. 2011, 59: 123–130.

64. Shafer RN. Prognosis of goniotomy in primary infantile glaucoma (trabecculodygenesis) Trans Am Ophthalmol Soc. 1982;80:321–325.

65. Russell-Eggitt IM, Rice NS, Jay B, Wyse RK. Relapse following goniotomy for congenital glaucoma due to trabecular dysgenesis. Eye (Lond). 1992, 6: 197–200.

66. Graham E, Tausch M, Kraemer C. Time of diagnosis, reoperations and long Term results of goniotomy in the treatment of primary congenital glaucoma: a clinical study. Int Ophthalmol. 1996-1997;20:117-123.

67. Sharaawy T., Bhartiya S. Surgical management of glaucoma: evolving paradigms. Indian J Ophthalmol. 2011, 59: 123–130.
complications of mitomycin C augmented trabeculectomy in refractory developmental glaucoma. Ophthalmic Surg Lasers. 1999; 30:473–80.

77. Fulcher T, Chan J, Lanigan B, Bowell R, O’Keefe M. Long-term follow-up of primary trabeculectomy for infantile glaucoma. Br J Ophthalmol. 1996, 80(6):499–502.

78. Freedman SF, McCormick K, Cox TA. Mitomycin C-augmented trabeculectomy with postoperative wound modulation in pediatric glaucoma. JAPOS. 1999, 3 (2):117–124.

79. Sidoti PA, Belmonte SJ, Liebmann JM, Ritch R. Trabeculectomy with mitomycin-C in the treatment of pediatric glaucomas. Ophthalmol. 2000,107 (3):422–429.

80. Waheed S, Ritterband DC, Greenfield DS, Liebmann JM, Sidoti PA, Ritch R. Bleb-related ocular infection in children after trabeculectomy with Mitomycin C. Ophthalmology. 1997, 104:2117–20.

81. Jayaram H, Scawn R, Pooley F. Long-term outcome of trabeculectomy augmented with Mitomycin C undertaken within the first two years of life. Ophthalmology. 2015, 122(11):2216–2222.

82. Ghafe D, Wang X. Surgical interventions for primary congenital glaucoma. Cochrane Database Syst Rev. 2015,1(CD008213).

83. Fang Y, Long Q, Guo W, Sun X. Profile of pediatric glaucoma patients in Shanghai Eye, Ear, Nose and Throat Hospital. Chin Med J (Engl) 2014, 127:1429–33.

84. Mandal AK, Gothwal VK, Nutheti R. Surgical outcome of primary developmental glaucoma: A single surgeon’s long-term experience from a tertiary eye care centre in India. Eye. 2007, 21:764–74.

85. 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. Ophthalmol. 2004; 111:283–90.

86. Sood D, Rathore A, Sood I, Singh G and Sood NN. Long-term outcome of combined trabeculectomy– trabeculotomy by a single surgeon in patients with primary congenital glaucoma. Eye (2018) 32, 426–432.

87. Helmy H Combined trabeculectomy-trabeculotomy versus Ahmed valve implantation for refractory primary congenital glaucoma in Egyptian patients: a long-term follow-up. Electronic Physician 2016, 8 (2):1884-91.

88. Dave P, Senthil S, Choudhari N, Sekhar GC. Outcomes of Ahmed valve implant following a failed initial trabeculotomy and trabeculectomy in refractory primary congenital glaucoma. Middle East Afr J Ophthalmol. 2015, 22 (1):64–68.

89. O’Malley Schotthoefer E, Yanovitch TL, Freedman SF. Aqueous drainage device surgery in refractory pediatric glaucomas: Long-term outcomes. J AAPOS. 2008; 12: 33-39.

90. Beck AD, Freedman S, Kammer J, Jin J. Aqueous shunt devices compared with trabeculectomy with Mitomycin-C for children in the first two years of life. Am J Ophthalmol. 2003; 136:994-1000.

91. Razeghinejad MR, Kaffashan S, Nowroozzadeh MH. Results of Ahmed glaucoma valve implantation in primary congenital glaucoma. J AAPOS. 2014; 18(6):590–595.

92. Werner M, Grajewski A. Further surgical options in children. In: Shaarawy TM, Sherwood MB, Hitchings RA, Crowston JG, editors. Glaucoma Surgical management. Vol. 2. Elsevier; 2009. pp. 507–9.

93. Chen TC, Bhatia LS, Walton DS. Ahmed Valve Surgery for Refractory Pediatric Glaucoma: A Report of 52 Eyes. J of Pediatric Ophthalmology and Strabismus. 2005; 42(5):274-283.

94. Chiang MY, Camuglia JE, Khaw PT. A Novel Method of Extending Glaucoma Drainage Tube: “Tube-in-Tube” Technique. J Glaucoma. 201, 26: 93-95.

95. Feusier M, Roy S, Mermoud A. Deep sclerectomy combined with trabeculectomy in pediatric glaucoma. Ophthalmology 2009,116 (1):30–8.

96. Luke C, Dietlein TS, Jacobi PC, Konen W, Krieglstein G K. Risk profile of deep sclerectomy for treatment of refractory congenital glaucomas. Ophthalmology.2002, 109:1066–1071.

97. Aquino M C, Barton K, Tan AM. Micropulse versus continuous wave transsceral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. Clin Experiment Ophthalmol. 2015; 43(1):40-46.

98. Elhefney, E. M., Mokbel, T. H., Hagras, S. M., AlNagdy, A. A., Ellayeh, A. A., Moshen, T. A., & Gafaa, W. M. Micropulsed diode laser cyclophotocoagulation in recurrent pediatric glaucoma. Eur J Ophthalmol. 2020; 30(5), 1149–1155.

99. Sood S and Beck AD. Cyclophotocoagulation versus sequential tube shunt as a secondary intervention following primary tube shunt failure in pediatric glaucoma. J Am Assoc for Ped Ophthalmol & Strabis 2009, 13(4): 379-38.

100. Lee EJ, Han, JC, Park DY, Kee C. Long-term morphologic fundus and optic nerve head pattern of progressive myopia in congenital glaucoma distinguished by age at first surgery. Sci Rep 2020,10, 10041.

101. Barsoum-Homisy M, Chevrette L. Incidence and prognosis of childhood glaucoma. Ophthalmology 1986; 93:1323-7.

102. Jin SW and Ryu WY. Clinical Manifestations of Strabismus in Patients with Primary Congenital Glaucoma. Seminars in Ophthalmology 2019, 34(6): 451-457.

103. Alsheikheh A, Klink J, Klink T, Steffen H, Grehn F. Long-term results of surgery in childhood glaucoma. Graefes Arch Clin Exp Ophthalmol. 2007; 245 (2):195–203.

104. Morales-Fernández L, Martínez-de-la-Casa J M , Benito-Pascual B, Saénz-Francés F, Santos-Bueso E, Arriola-Villalobos P , Escribano-Martínez J, García-Feijo J. Cataract extraction in patients with primary congenital glaucoma Eur J Ophthalmol. 2020, 30(3):525-532.

105. Khokhar S, Yadav D, Gupta S, Sihota R, Chaurasia AK, Gupta A, Gupta V. Refractive outcomes of cataract surgery in primary congenital glaucoma Eye (Lond) 2019 Apr;33(4):542-548.

Cite This Article as: Arshi Singh., Kirti Singh. Primary congenital glaucoma: An update Delhi J Ophthalmol 2021; 32 (2): 7 - 13.

Acknowledgments: Nil

Conflict of interest: None declared

Source of Funding: None

Date of Submission: 21 Nov 2021
Date of Acceptance: 06 Dec 2021

Address for correspondence

Arshi Singh Senior Resident
Department of Ophthalmology, Guru Nanak Eye Centre, New Delhi, India.
E-mail: arshising@hotmail.com

Quick Response Code