Advances in Ophthalmology Practice and Research 4 (2024) 216–219

Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

journal homepage: www.journals.elsevier.com/advances-in-ophthalmology-practice-and-research

Letter to the Editor

Clinical outcome of sequential bilateral pediatric penetrating keratoplasty (PKP) in patients with corneal dystrophies in South India

Dear Editor,

Penetrating keratoplasty (PKP) in pediatric corneal blindness (<18 years of age) is the standard surgical procedure for visual rehabilitation in full thickness corneal scarring and to avoid deprivation amblyopia.[1]

Congenital corneal opacities account for higher number of pediatric PKP in the western world as compared to India where it's more of corneal leucoma post microbial keratitis.[2] Congenital hereditary endothelial dystrophy, congenital glaucoma and macular corneal dystrophy (MCD) are the more common indications for pediatric PKP in the gulf, middle east countries because of higher rate of consanguineous marriages.[3,4]

Al-Ghamdi et al. from Saudi Arabia reported as high as 80% of pediatric PKP performed for congenital opacities out of which 2/3rd was because of congenital glaucoma & CHED.[4] CHED should be differentiated from congenital glaucoma as has been cautioned in the reports of misdiagnosis.[5]

Pediatric PKP is a surgical challenge due to difficult pre-operative work up and intra-operative hurdles like smaller eyes, positive posterior pressure, frequent post-operative evaluation under anaesthesia.[6,7] However, bilateral PKP in paediatric age group has shown favourable results in recent times.[8,9] The prognosis of corneal grafting has improved due to the ever-improving quality of eye banking, advancement in surgical techniques, improved management of complications.

However, there is limited literature on the outcome following sequential bilateral pediatric PKP in patients with corneal dystrophies in India. We retrospectively analysed the visual outcome, graft clarity and complications following sequential bilateral paediatric PKP for corneal dystrophies performed at our centre in Southern India.

This was a retrospective, observational study which included 32 eyes of 16 pediatric patients (<18 years) with corneal dystrophy who underwent bilateral PKP between August 2016 to June 2019 and follow up for at least one year post second eye surgery.

Unilateral keratoplasty, lamellar and therapeutic keratoplasty and patients with less than 1 year of follow up were excluded. Preoperative workup included demographic, best corrected visual acuity (BCVA) and ocular examination findings. The indication for keratoplasty, details of the surgery and of any additional procedure were recorded. Examination under anaesthesia was done in younger, uncooperative cases and pre op. intravenous mannitol (1 gm/kg body weight) was given in most patients. Post-operatively, outcome, graft clarity, complications, were recorded and analysed. The eye with better visual potential was operated first. The donor graft size was oversized by 0.5 mm and 10-0 nylon monofilaments sutures (Ethicon) were used for suturing. Flieringa ring was used in many cases to avoid possible globe collapse due to low scleral rigidity. Suture removal was done any time from 7 months to 1 year, and early suture removal was done in patients with loose sutures or high astigmatism.

Post-operative treatment included systemic steroid (1 mg/kg/day body wt), topical steroid eye drops (Prednisolone acetate 1% eye drops). Topical steroids were started at 4 times a day for 1 month tapered to 3 times a day for a month followed by 2 times a day. Oral steroids are indicated in repeat grafts and usually not given in the primary surgery, but we have used oral steroids to compensate for the non-compliance and unreliable follow up. Post bilateral PKP, graft rejection in first operated eye is significantly increased after second eye surgery. Before operating the second eye for keratoplasty, the frequency of topical steroids in the first eye should be increased to around six times a day tapered to 4, 3, 2 times a day 3 weekly each. Also, topical steroids were increased to 4 times a day at the time of scheduled vaccination (one week before and after) in the operated eye. Patients who developed steroid induced raised IOP, we shifted to flurometholone eye drops, added topical cyclosporine and tacrolimus ointment.

Topical antibiotic eye drops 4 times and cycloplegic (cyclopentolate) eye drops 3 times a day as per protocol. Patients were followed up at monthly intervals till sutures were on and 2 monthly after complete suture removal.

We performed statistical analysis using Chi-square test, paired '*t*' test and student '*t*' test to analyse the data.

The mean age was 13.7 ± 4.46 years at the time of surgery and male: female ratio was 9:7. As CHED presents early during critical visual development period, early PKP in CHED is preferred to prevent amblyopia.[4] Macular corneal dystrophy patients usually need surgery at later stages of 3rd or 4th decade of life, but there are patients who require early surgery as well. Mean time interval between the two eyes surgery was 26.31 ± 34.24 months. The mean pre-operative vision was 1.504 ± 0.584 logMAR and mean post-operative vision was 0.813 ± 0.551 logMAR in our study. There was a significant visual improvement post-PKP in our study at 1year follow-up. ($P < 0.001$) (Table 1a). In both first and second eye operated groups separately, there was significant improvement in vision ($P = 0.0098$; $P = 0.018$) (Table 1b) and significant improvement in vision was seen in CHED cases ($P = 0.009$) which was not significant in MCD ($P = 0.201$). In our study, graft clarity was noted in 87.5% of the eyes and 12.5% of the grafts failed at 1 year follow up (Fig. 1). Two patients had poor vision despite clear graft due to unilateral cataract, nystagmus, exotropia and amblyopia. PKP in CHED cases has shown excellent outcome as compared to PKP for other pathologies.[3] PKP in MCD has graft survival recorded to be as high as 87%–92%.[10–12]

Graft rejection was the most common of complications encountered post PKP (50%) followed by secondary glaucoma, graft failure, keratitis (fungal), cataract and graft dehiscence(Table 2 a). This is similar to

https://doi.org/10.1016/j.aopr.2024.09.003
Received 22 June 2024; Received in revised form 19 September 2024; Accepted 26 September 2024
Available online 27 September 2024

Table 1
(a) Comparison of preoperative and postoperative BCVA (LogMAR) at one-year follow-up; (b) Comparison of Pre Op. & Post Op. vision between First Eye & Second Eye.

Table 1 (a)

No of eyes	Pre-op. BCVA log MAR		Post-op. BCVA log MAR		Mean Difference	SE	*P* value
32	Mean 1.504	SD 0.584	Mean 0.813	SD 0.551	0.691	0.084	< **0.001***

Table 1 (b) BCVA	Pre op vision	Postop vision	*P* value	Pre op vision	Postop vision	*P* value
≥ 6/12; 6/18–6/60; < 6/60	First op. eye (n = 16)		**0.0098***	Second op. eye (n = 16)		**0.018***

Table 1 (c)						
≥ 6/12; 6/18–6/60; < 6/60	CHED (n = 24)		**0.009***	MCD (n = 8)		0.201

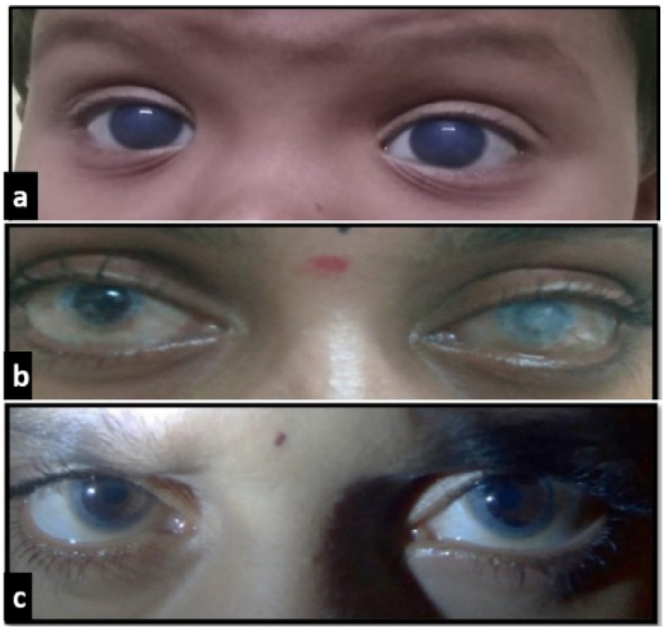

Fig. 1. (a). CHED in 6 year old child at presentation.
(b). Right eye clear graft, Left eye failed graft post-PKP.
(c). Bilateral Clear Cornea post-PKP in a 12 year patient.

previous published data.[4,12] Statistically significant difference (*P* = 0.003*) was observed between rejection in first (10 eyes) and second (2 eyes) eye PKP (Table 2 b). Incidence of graft rejection in paediatric corneal grafts varies from 12.1% to 43.4%.[3,5] In pediatric cases, around 25%–28% corneal grafts show reversal from rejection as compared to much higher reversal in adult grafts (50–78%).[3,13] This could be because of the more active immune system in younger patients causing higher postoperative inflammation.[14] When presented early, it can be managed well with prompt corticosteroid treatment. Although reversal of graft rejection in our cases was 8/12 (66.67%), most cases presented late than expected after initial symptoms observed at home. 4 of 12 eyes (33.33%) had subsequent graft failure (Table 2a).

In the literature from western developed nations, rejection has not been seen to be a significant predictor of graft failure.[15] However,

Table 2
(a) Complications as seen in first, second eye PKP. (b) Graft Rejection in first, second eye PKP.

2 (a) Complications	First eye (16): n	Second eye (16): n	Total (%)	*P* value
Graft rejection	10	2	12(50.0%)	**0.003***
Secondary glaucoma (steroid induced)	2	2	4(16.67%)	1.000
Graft failure	4	0	4(16.67%)	0.101
Fungal keratitis	2	0	2(8.33%)	0.483
Blunt ocular trauma, Graft dehiscence	1, 1	0, 0	1(4.17%) each	1.000 each

2 (b) Graft Rejection (n = 12)	Number (n)	Total (%)	
First operated eyes rejection before second eye PKP	1	8.33	**0.005***
First operated eyes rejection after second eye PKP; following IOL	8; 1	66.67; 8.33	
Second eye PKP Rejection	2	16.67	

delayed presentation of graft rejection as also observed by us can be a significant cause of subsequent graft failure.[3,16] Both categories of patients from rural background and parents of pediatric corneal graft recipients are at risk of delayed presentation and should be educated, more aggressively counseled for subtle, early symptoms to ensure early management.[3,16]

In our series, more number of larger (≥8 mm) grafts had rejections (8 of 17 eyes, 47.1%) as compared to smaller (<8 mm grafts) grafts (4 of 15, 26.7%). (*P* = 0.235) Probably, future studies with larger sample size may help in studying this association further.

Bilateral PKP in patients with corneal dystrophy provide favourable outcome. The ideal time for the second eye PKP is after atleast 6 months duration. Although the interval between two eyes surgery was 8–12 months in majority of our patients (12, 75%), 4 patients (25%) had inter PKP durations of 92, 37, 59 and 119 months. Due to presence of these outliers the mean inter eye duration was 26.31 ± 34.24 months. Rao et al. found corneal transplantation in the second eye did not increase the risk of graft rejection in either eye in adults.[8] However, in our study there was an increased risk of rejection in the first operated eye following subsequent eye PKP surgery as seen in most eyes (n = 8/12; 66.67%) and this showed significant impact of second eye graft on the rejection in first operated eye (*P* = 0.005***)**, (Table 2b). As discussed earlier, the frequency of topical steroids in the first eye were increased to around six times a day, tapered to 4, 3, 2 times a day 3 weekly each before operating the second eye.[17]

Systemic sensitisation to mismatched tissue histocompatibility antigens in the two grafts may have an important role to play in this increased risk of graft rejection.[17,18] Vail A et al. reported an increased tendency of graft rejection in patients who underwent subsequent eye PKP.[19] However, "apparent enhanced survival" of the second eye graft probably due to better post-op. care of the second eye, improved surgical technique, selection bias and state of relative anergy after first graft cannot be ignored.[8,20]

PKP (without any other procedure) was done in 22 eyes (68.75%), 4 eyes (12.5%) required PKP with cataract surgery (+IOL) in same sitting and 6 underwent cataract surgery following PKP (of which 2 were left aphakic). We performed cornea triple surgery if cataract was significant enough, otherwise we avoid multiple surgeries at the time of corneal grafting. Glasses correction was given 1 month after PKP, and we used glasses and occlusion of the other eye to treat amblyopia in aphakic cases.

In our study, only 1 eye had an episode of graft rejection following cataract performed after PKP surgery, which responded well to treatment with topical steroid. An increased rate of graft failure in eyes which had additional surgical procedures were performed after PKP, was noted by

some studies.[21,22] The limitation in this study was its retrospective nature, small sample size, short term follow up especially in second operated eye with first eye having longer follow up as it was operated much earlier.

Nowadays, CHED cases are considered for endothelial keratoplasty and most cases of macular dystrophy are considered for deep anterior lamellar keratoplasty. However, traditionally PKP is the surgery of choice in CHED.[1] Currently DSAEK is the treatment of choice for endothelial disease in adults and its advantages over PKP include a closed chamber surgery, very few sutures and lesser post surgery astigmatism.[23] DSAEK in pediatric age group also has advantages of lesser incidence of graft rejection, suture related complications and lesser need for examination under anaesthesia as compared to PKP.[24,25] However, in pediatric age group, DSAEK is a surgical challenge because of intra-operative difficulties faced like poor visibility, strong adherence of Descemet membrane to posterior stroma which may lead to retained DM and failed graft.[24,26] Although the long term graft survival and visual recovery in DSAEK has been seen to be superior to PKP, but PKP is still superior to DSAEK in terms of attaining "pristine graft clarity" especially in CHED cases.[23,27,28] Continuous evolution and ever improving surgical skills in DSAEK may soon replace PKP as standard procedure in such cases but still PKP will remain an important choice in severe pediatric endothelial disease.[1,25] The patients in our cohort are often from far off rural locations and from lower literacy, socio-economic groups so educating them about importance of amblyopia therapy and regular follow up is still the need of the hour. Pediatric PKP needs to be closely monitored with better awareness, aggressive counselling on the warning signs/symptoms to prevent graft failure and permanent visual damage.

Study approval

The authors confirm that any aspect of the work covered in this manuscript that involved human patients or animals was conducted with the ethical approval of all relevant bodies and the study was performed in accordance with the Declaration of Helsinki.

Author contributions

Rekha Gyanchand, Mamatha B, Salma Mohd Iqbal Tabani: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review and editing.

Rajan Sharma, Ashok Sharma: Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review and editing.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Vanathi M, Panda A, Vengayil S, Chaudhuri Z, Dada T. Pediatric keratoplasty. *Surv Ophthalmol*. 2009 Mar-Apr;54(2):245–271. https://doi.org/10.1016/j.survophthal.2008.12.011. PMID: 19298903.
2. Kusumesh R, Vanathi M. Graft rejection in pediatric penetrating keratoplasty: clinical features and outcomes. *Oman J Ophthalmol*. 2015 Jan-Apr;8(1):33–37. https://doi.org/10.4103/0974-620X.149862. PMID: 25709272; PMCID: PMC4333541.
3. Al-Rajhi AA, Wagoner MD. Penetrating keratoplasty in congenital hereditary endothelial dystrophy. *Ophthalmology*. 1997 Jun;104(6):956–961. https://doi.org/10.1016/s0161-6420(97)30200-0. PMID: 9186436.
4. Al-Ghamdi A, Al-Rajhi A, Wagoner MD. Primary pediatric keratoplasty: indications, graft survival, and visual outcome. *J AAPOS*. 2007 Feb;11(1):41–47. https://doi.org/10.1016/j.jaapos.2006.09.012. PMID: 17307682.
5. Javadi MA, Baradaran-Rafii AR, Zamani M, et al. Penetrating keratoplasty in young children with congenital hereditary endothelial dystrophy. *Cornea*. 2003 Jul;22(5):420–423. https://doi.org/10.1097/00003226-200307000-00006. PMID: 12827046.
6. Aasuri MK, Garg P, Gokhle N, Gupta S. Penetrating keratoplasty in children. *Cornea*. 2000 Mar;19(2):140–144. https://doi.org/10.1097/00003226-200003000-00004. PMID: 10746443.
7. Sharma A, Sharma R. Pediatric corneal transplant surgery: challenges for successful outcome. *Nepal J Ophthalmol*. 2019 Jul;11(22):197–210. https://doi.org/10.3126/nepjoph.v11i2.27828. PMID: 32792704.
8. Rao SK, Sudhir RR, Fogla R, Rajagopal R, Sitalakshmi G, Padmanabhan P. Bilateral penetrating keratoplasty–indications, results and review of literature. *Int Ophthalmol*. 1999;23(3):161–166. https://doi.org/10.1023/a:1010635231828. PMID: 11456254.
9. Majander A, Kivelä TT, Krootila K. Indications and outcomes of keratoplasties in children during a 40-year period. *Acta Ophthalmol*. 2016 Sep;94(6):618–624. https://doi.org/10.1111/aos.13040. Epub 2016 Apr 7. PMID: 27061670.
10. Al-Swailem SA, Al-Rajhi AA, Wagoner MD. Penetrating keratoplasty for macular corneal dystrophy. *Ophthalmology*. 2005 Feb;112(2):220–224. https://doi.org/10.1016/j.ophtha.2004.08.017. PMID: 15691554.
11. Pandrowala H, Bansal A, Vemuganti GK, Rao GN. Frequency, distribution, and outcome of keratoplasty for corneal dystrophies at a tertiary eye care center in South India. *Cornea*. 2004 Aug;23(6):541–546. https://doi.org/10.1097/01.ico.0000126324.58884.b9. PMID: 15256989.
12. Writing Committee for the Cornea Donor Study Research Group, Sugar A, Gal RL, Kollman C, et al. Factors associated with corneal graft survival in the cornea donor study. *JAMA Ophthalmol*. 2015 Mar;133(3):246–254. https://doi.org/10.1001/jamaophthalmol.2014.3923. PMID: 25322173; PMCID: PMC4394864.
13. Alldredge OC, Krachmer JH. Clinical types of corneal transplant rejection. Their manifestations, frequency, preoperative correlates, and treatment. *Arch Ophthalmol*. 1981 Apr;99(4):599–604. https://doi.org/10.1001/archopht.1981.03930010599002. PMID: 7013739.
14. Gulias-Cañizo R, Gonzalez-Salinas R, Hernandez-Zimbron LF, Hernandez-Quintela E, Sanchez-Huerta V. Indications and outcomes of pediatric keratoplasty in a tertiary eye care center: a retrospective review. *Medicine (Baltim)*. 2017 Nov;96(45):e8587. https://doi.org/10.1097/MD.0000000000008587. PMID: 29137083; PMCID: PMC5690776.
15. Dana MR, Moyes AL, Gomes JA, et al. The indications for and outcome in pediatric keratoplasty. A multicenter study. *Ophthalmology*. 1995 Aug;102(8):1129–1138. https://doi.org/10.1016/s0161-6420(95)30900-1. PMID: 9097737.
16. Sharma R, Mamatha B, Sharma S, Gyanchand R. Impact of pandemic COVID-19 lockdown on penetrating keratoplasty patients. *Indian J Ophthalmol*. 2023 Jan;71(1):95–100. https://doi.org/10.4103/ijo.IJO_1190_22. PMID: 36588216; PMCID: PMC10155521.
17. Coster DJ, Williams KA. The impact of corneal allograft rejection on the long-term outcome of corneal transplantation. *Am J Ophthalmol*. 2005 Dec;140(6):1112–1122. https://doi.org/10.1016/j.ajo.2005.07.024. PMID: 16376660.
18. Williams KA, Kelly TL, Lowe MT, Coster DJ. All contributors to the Australian Corneal Graft Registry. The influence of rejection episodes in recipients of bilateral corneal grafts. *Am J Transplant*. 2010 Apr;10(4):921–930. https://doi.org/10.1111/j.1600-6143.2009.03002.x. Epub 2010 Feb 1. PMID: 20121748.
19. Vail A, Gore SM, Bradley BA, Easty DL, Rogers CA. Corneal graft survival and visual outcome. A multicenter study. Corneal transplant follow-up study collaborators. *Ophthalmology*. 1994 Jan;101(1):120–127. https://doi.org/10.1016/s0161-6420(94)31376-5. PMID: 8302544.
20. Tuft SJ, Gregory WM, Davison CR. Bilateral penetrating keratoplasty for keratoconus. *Ophthalmology*. 1995 Mar;102(3):462–468. https://doi.org/10.1016/s0161-6420(95)30999-2. PMID: 7891986.
21. Steger B, Curnow E, Cheeseman R, et al. National health service blood and transplant ocular tissue advisory group and contributing ophthalmologists (OTAG audit study 21). Sequential bilateral corneal transplantation and graft survival. *Am J Ophthalmol*. 2016 Oct;170:50–57. https://doi.org/10.1016/j.ajo.2016.07.019. Epub 2016 Aug 1. PMID: 27491697.
22. Schaumberg DA, Moyes AL, Gomes JA, Dana MR. Corneal transplantation in young children with congenital hereditary endothelial dystrophy. Multicenter Pediatric Keratoplasty Study. *Am J Ophthalmol*. 1999 Apr;127(4):373–378. https://doi.org/10.1016/s0002-9394(98)00435-8. PMID: 10218688.
23. Mehta N, Ramappa M. Novel proposed algorithm in congenital hereditary endothelial dystrophy. *Semin Ophthalmol*. 2023 Feb;38(2):108–115. https://doi.org/10.1080/08820538.2022.2094713. Epub 2022 Jun 28. PMID: 35763407.
24. Pineda R 2nd, Jain V, Shome D, Hunter DC, Natarajan S. Descemet's stripping endothelial keratoplasty: is it an option for congenital hereditary endothelial dystrophy? *Int Ophthalmol*. 2010 Jun;30(3):307–310. https://doi.org/10.1007/s10792-009-9315-x. Epub 2009 Jul 19. PMID: 19618126.
25. Ashar JN, Ramappa M, Vaddavalli PK. Paired-eye comparison of Descemet's stripping endothelial keratoplasty and penetrating keratoplasty in children with congenital hereditary endothelial dystrophy. *Br J Ophthalmol*. 2013 Oct;97(10):1247–1249. https://doi.org/10.1136/bjophthalmol-2012-302602. Epub 2013 Apr 23. PMID: 23613513.
26. Asif MI, Bafna RK, Sharma N, et al. Microscope integrated optical coherence tomography guided Descemet stripping automated endothelial keratoplasty in

congenital hereditary endothelial dystrophy. *Clin Ophthalmol*. 2021 Jul 27;15: 3173–3181. https://doi.org/10.2147/OPTH.S300286. PMID: 34349494; PMCID: PMC8326941.
27. Ramappa M, Mohamed A, Achanta DSR, Tumati CSK, Chaurasia S, Edward DP. Descemet stripping automated endothelial keratoplasty in pediatric age group: a decade of our experience. *Cornea*. 2021 Dec 1;40(12):1571–1580. https://doi.org/10.1097/ICO.0000000000002811. PMID: 34320595.
28. Sharma N, Agarwal R, Jhanji V, Bhaskar S, Kamalakkannan P, Nischal KK. Lamellar keratoplasty in children. *Surv Ophthalmol*. 2020 Nov-Dec;65(6):675–690. https://doi.org/10.1016/j.survophthal.2020.04.002. Epub 2020 Apr 17. PMID: 32305350.

Rekha Gyanchand, B. Mamatha, Salma Mohd Iqbal Tabani, Rajan Sharma*
B.W. Lions Superspeciality Eye Hospital, Bengaluru, India

Ashok Sharma
Cornea Centre, Chandigarh, U.T, India

* Corresponding author. Cornea Centre, Chandigarh, U.T, India.
E-mail address: rajansharma122@gmail.com (R. Sharma).