


A Case Report of Congenital Corneal Opacity: Challenges of Keratoplasty Surgery in Children

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ABSTRACT

Introduction: Congenital corneal opacity (CCO) is a group of anterior segment dysgenesis of the eye manifested by corneal transparency loss at birth or during the first 4 weeks of life. CCO is one of the most prominent disease entities in anterior segment dysgenesis. CCO resulted from disruptions in mesodermal development, particularly affecting the anterior segment of the eye**. Case:** A 2-week-old boy with bilateral CCO. One week post-keratoplasty surgery, the parents reported no complaints but had difficulty administering eye drops. Physical examination showed a clearer corneal graft. One month later, a cloudy graft and broken sutures were noted, indicating graft rejection. The family was educated on the importance of consistent medication for any future graft surgery. **Discussion:** The surgical option for CCO is corneal graft or keratoplasty. Keratoplasty is a corneal transplant where a clear donor graft replaces the central opaque cornea. **Conclusion:** A comprehensive workup is essential for diagnosing CCO. Keratoplasty can restore corneal clarity and vision, but pediatric cases require careful patient education and comprehensive follow-up.

Keywords: Anterior segment dysgenesis, case report, congenital corneal opacity, corneal graft, keratoplasty.

ABSTRAK

Pendahuluan: Opasitas kornea kongenital atau *congenital corneal opacity* (CCO) adalah sekelompok disgenesis segmen anterior yang ditandai dengan hilangnya transparansi kornea sejak lahir atau dalam 4 minggu pertama kehidupan. CCO merupakan salah satu entitas penyakit yang paling menonjol dalam disgenesis segmen anterior. CCO disebabkan oleh gangguan dalam perkembangan mesodermal, terutama memengaruhi segmen anterior mata. **Kasus:** Neonatus laki-laki berusia 2 minggu dengan CCO bilateral. Satu minggu pasca-operasi keratoplasti, orang tua pasien melaporkan tidak ada keluhan, namun pemberian obat tetes mata sulit karena pasien tidak kooperatif. Pemeriksaan fisik menunjukkan *graft* kornea yang lebih jernih. Satu bulan kemudian, ditemukan *graft* keruh dan beberapa jahitan lepas, yang mengindikasikan penolakan *graft*. Keluarga pasien telah diedukasi tentang pentingnya penggunaan obat secara konsisten untuk operasi *graft* di masa mendatang. **Diskusi:** Pilihan bedah untuk CCO adalah cangkok kornea atau keratoplasti. Keratoplasti adalah transplantasi kornea di mana cangkok donor yang bening menggantikan kornea sentral yang buram. **Simpulan:** Pemeriksaan menyeluruh sangat penting dalam diagnosis CCO. Keratoplasti dapat mengembalikan kejernihan kornea dan penglihatan, namun pada kasus pediatrik diperlukan edukasi pasien yang lebih cermat dan pemantauan lanjutan yang komprehensif. **Dian Estu Yulia, Yura Pradiptama, Sabrina Tan. Sebuah Laporan Kasus Opasitas Kornea Kongenital: Tantangan Keratoplasti pada Anak.**

Kata Kunci: Disgenesis segmen anterior, laporan kasus, opasitas kornea kongenital, *graft* kornea, keratoplasti.

INTRODUCTION

Congenital corneal opacity (CCO) is a group of diseases manifested by loss of transparency in the corneal tissue at birth or during the first four weeks of life. This condition is associated with disturbances during anterior segment differentiation between the 6th and 16th weeks of gestation.[1,2] In the USA, approximately 3 in every 100,000 neonates are born with CCO. An Indonesian study reports that corneal opacity was the most common manifestation of anterior segment dysgenesis, representing 55.8% of cases.[3] One study reported a male-to-female ratio of 1.7:1. However, other studies do not report a significant gender difference, suggesting variability depending on the population and condition studied.[1,3,4] Most cases are diagnosed within the first year of life. A study in Minnesota showed that

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the mean age is 7.5 months, whereas in Indonesia, it is 3.4 years old.[3,5]

CCO is one of the most prominent disease entities in anterior segment dysgenesis. CCO resulted from disruptions in mesodermal development, particularly affecting the anterior segment of the eye.[6] CCO may obstruct the visual axis and hinder the development of eyesight. CCO can be caused by numerous factors, such as infection, genetic or metabolic conditions, developmental disorders, trauma, intoxication, and idiopathic origins.[7]

Diagnosing CCO poses a challenge for clinicians. A detailed history covering birth details, growth and development of the patient, and family history needs to be evaluated. A thorough systemic evaluation and ocular examination are essential to identify any associated disorders.[4,8,9] By integrating these aspects, clinicians can accurately identify the underlying cause of corneal opacity and tailor treatment strategies to each patient's specific condition.

CCO management requires a comprehensive and cautious approach, as the choice of therapy differs between unilateral and bilateral CCO. In unilateral CCO, the decision to perform corneal grafting should be carefully evaluated based on factors such as the status of the fellow eye and potential visual acuity outcomes. Preserving vision in the affected eye and preventing blindness with patching are more applicable in unilateral conditions. On the other hand, the goal of bilateral corneal opacity treatment is to restore binocular vision as early as possible. Keratoplasty is a common choice in this condition to prevent blindness as soon as possible. However, keratoplasty in pediatric patients is rarely performed due to a high risk of graft failure and often poor visual outcomes. Challenges in pediatric keratoplasty include complex preoperative evaluation, intraoperative obstacles, and post-operative management after follow-up.[10,11] Keratoplasty surgical rates for CCO differ across regions. In Asia-Pacific, studies by Shi, *et al*., and Chang, *et al*., found that keratoplasty was performed in 12.9% and 5.5% of CCO cases, respectively.[12,13] In New Zealand, Patel, *et al*., found that 16% of keratoplasties were indicated for CCO.[14]

Prognosis after corneal transplantation in CCO cases appears promising. A retrospective study from Michaeli, *et al*., reported that 78% of children achieved corneal clarity after corneal transplantation, though this was achieved with repeated transplants.[15] Corneal graft rejection in children is higher than in adults, requiring closer observation to identify any signs of rejection in the cornea. Late recognition, failure to follow up regularly, and late presentation to the health center adversely disturbed the graft outcome.[10,11,15] The challenges may cause delays and even omissions in diagnosis and treatment, resulting in visual impairment; this may even jeopardize the overall development of children.[2,16]

CASE

A two-week-old baby boy presented to Cipto Mangunkusumo General Hospital with a chief complaint of a white lesion in the cornea of both eyes since birth. His parents noted that the patient frequently closes his eyes in response to light. The patient was born full-term, appropriate for gestational age, via cesarean section. There was a history of fever during pregnancy. The patient is breastfeeding well, with no other abnormalities except the white lesions in the eyes. The patient is the second child out of two siblings. The older sibling does not have similar complaints. There is no family history of eye diseases. No systemic abnormalities were found in the patient.

The ocular examination showed a blink reflex in both eyes, and no nystagmus was observed. Examination of the anterior segment revealed a corneal size of 10 mm in both eyes, with corneal opacity (**Figure 1**) resembling scleral tissue on the surface and no signs of injection. The patient underwent an ultrasound examination to assess the condition of the eyeballs further. The axial length was 18 mm in the right eye and 20 mm in the left eye, with no abnormalities in the posterior segment. The patient was diagnosed with corneal opacity in both eyes. Keratoplasty was considered a potential intervention due to bilateral corneal opacity, with a plan for keratoplasty once the patient reaches one year of age. The patient was subsequently placed on the waiting list for a corneal donor for keratoplasty in the right eye.

The patient finally received a corneal donor and underwent keratoplasty under general anesthesia, fully funded by the government. During surgery, pachymetry was performed to identify the depth of the lesion. The depth of the lesion was 800 µm, and the corneal thickness was 900 µm, indicating endothelial cell involvement. Thus, it was decided to perform keratoplasty. Post-operatively, the patient was prescribed oral and eye drop antibiotics and anti-inflammatory medications. On the first post-operative day, the patient could follow objects and lights. Subconjunctival hemorrhage was observed inferiorly. The corneal graft appeared cloudy, but no

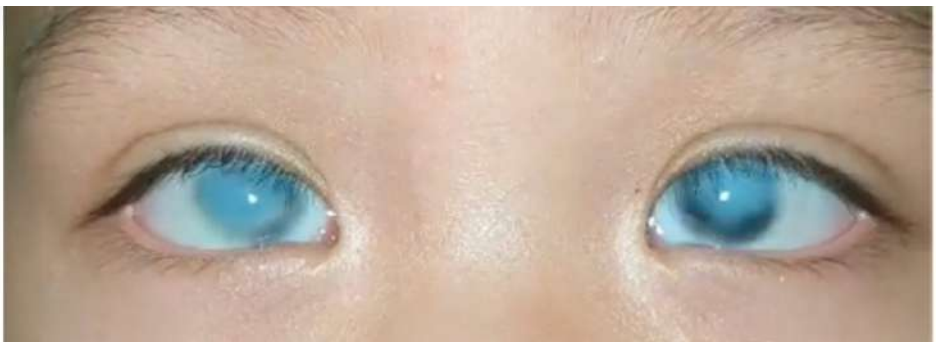

Photo documentation by dr. Dian Estu Yulia

Figure 1. Pre-operative clinical presentation revealed corneal opacity in both eyes, with the right eye showing more extensive surface involvement.

staining was observed on the surface, and the sutures on the cornea were intact. The patient's cooperation issues made it difficult to assess other areas of the eye. The patient was scheduled for a follow-up appointment in one week and had no complaints, but administering eye drops was challenging due to the child's non-cooperation. Physical examination revealed reduced subconjunctival hemorrhage, a clearer appearance of the grafted cornea, and improved visibility of the iris and pupil, with a hint of pupil decentration towards 7 o'clock. As the condition improved, medication was tapered down. The patient was then scheduled for a follow-up appointment in two weeks.

Unfortunately, the patient returned to the clinic one month after the keratoplasty procedure, presenting with deteriorating eye conditions. His parents reported difficulties in administering medication and managed to give drops only at night. The right eye became cloudy, and it was unclear whether the patient had previously rubbed the eye. Additionally, the patient ceased wearing the eye shield. Upon ocular examination, conjunctival and scleral injections were noted, along with a cloudy corneal graft and several broken sutures from 10 o'clock to 6 o'clock, suggesting graft displacement. The patient was suspected of corneal graft rejection one month post-keratoplasty. As a result, the patient was planned for a re-suturing procedure of the right eye graft under anesthesia. During the re-suturing procedure, it was decided to remove all nylon sutures from the graft due to signs of graft failure. Post-operatively, the patient was prescribed oral and eye drop antibiotics and anti-inflammatory medications. At the one-week follow-up, reduced edema was observed, but corneal opacity persisted, and no neovascularization was noted. The patient was instructed to return for a one-month follow-up with the same medication regimen.

One month after the last procedure, the patient returned for a follow-up appointment and was reportedly compliant with regular eye drop use. The patient could recognize colors, see fingers, and count from a close distance (0.5 meters). The patient appeared happy when seeing lights and objects. However, neovascularization was observed across all quadrants, particularly in the superior quadrant on the cloudy cornea. The pupil detail appeared round. The patient was diagnosed with corneal graft failure in the right eye. His family was educated about the complexity of corneal graft surgery and the possibility of future graft surgery. The eye condition of the patient at each post-operative visit is seen in **Figure 2**.

DISCUSSION

In evaluating the cornea, it is crucial to determine whether the opacity is bilateral or unilateral, the degree and depth of opacity, corneal thickness, and anterior chamber depth. Slit lamp examination and tomographic imaging are crucial for views of the chamber angle, iris, and lens with any adhesions. Younger patients often cannot be examined thoroughly due to the inability to sit still and the tendency to cry. Direct eye contact examination procedures, like pachymetry, are essential in diagnosing corneal opacity.[4,8,9]

A detailed slit-lamp examination of the anterior segment is necessary to assess for any additional signs of anterior segment dysgenesis. In our case, due to the patient's young age, it is challenging to assess the ocular condition directly on the slit-lamp. Ultrasonography could help evaluate the posterior segment of the eye. However, the anterior chamber assessment was complex due to the patient's limited cooperation. As a result, the clinical appearance served as the primary basis for our evaluation. The patient was evaluated for any underlying systemic disorder and underwent echocardiography, head ultrasound, and TORCH (toxoplasmosis, others [syphilis, varicella zoster virus], rubella, cytomegalovirus, and herpes simplex virus) infection markers, and the results were within normal limits. Echocardiography was carried out to explore any congenital heart defects.

Corneal opacity has resulted in severe visual impairment in both eyes. Early intervention is crucial for visual rehabilitation and preventing lifelong visual disability. The management of CCO focuses on improving visual acuity and preventing blindness. Treatment options include medical and surgical management. Medical management includes treating underlying conditions if identified.

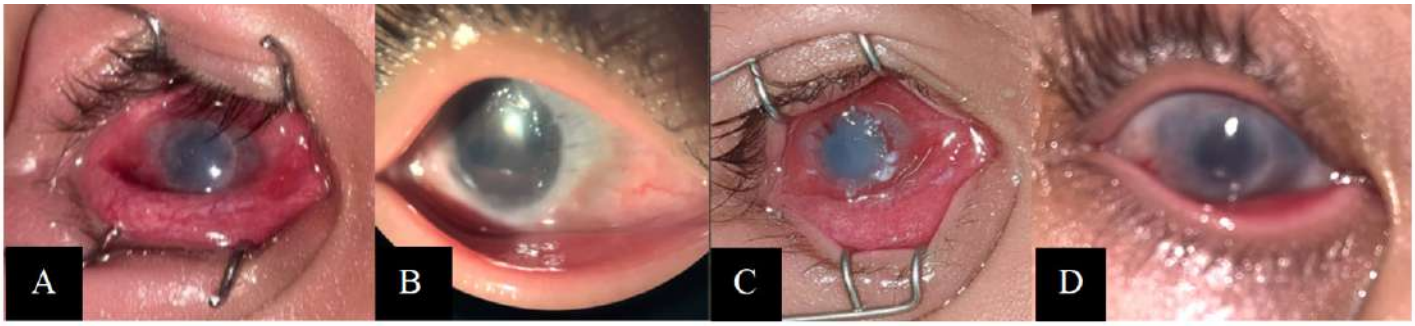

Photo documentation by dr. Dian Estu Yulia

Figure 2. Eye condition of the patient at each post-operative visit. **A.** Day one post-operative: The cornea appeared relatively clear, with all sutures intact and no signs of loose sutures or breakage. **B.** One week post-operative: The cornea remained clear, allowing detailed visualization of the anterior chamber. **C.** Three weeks post-operative: The condition had deteriorated, with the cornea becoming hazy and some sutures appearing loose, suggesting signs of graft failure. **D.** One week after removal of all sutures: Corneal haze persisted, confirming the diagnosis of corneal graft failure.


Lubricants can help relieve corneal surface dryness and discomfort. Antibiotics and anti-inflammatory medications may also be administered to manage infections or vascularization if present.[2,17]

The surgical option for CCO is a corneal graft or keratoplasty. Keratoplasty is a corneal transplant where a clear donor graft replaces the central opaque cornea. During the surgery, anterior segment optical coherence tomography (AS-OCT) revealed a lesion depth indicating the involvement of the endothelial cells. Based on these findings, the patient proceeds with keratoplasty. Keratoplasty in infants is carried out when there are indications, such as a significant corneal opacity impairing vision, risk of blindness, and failure of medical therapy.[18,19] Advancements in surgical techniques, improved understanding of risk factors that may assist in predicting and avoiding unfavorable results, and improved post-operative care have led to an increased success of pediatric keratoplasties.[18–20]

The prognosis of the corneal graft in CCO depends on timely intervention, the underlying cause, and post-operative management. Early intervention leads to better visual outcomes due to reduced risk of blindness.[18,21,22] While most research indicates that older children have higher survival rates, there is disagreement over the best time for keratoplasty. According to Lowe, *et al*., teenagers aged 13–19 years old showed higher corneal transplant survival than younger age groups, whereas infants under 5 years old showed worse graft survival than children 5–12 years old.[23] In contrast, Karadag, *et al*., discovered that early surgery was not linked to an increased risk of graft failure in children 12 years of age and younger.[24] Studies in China reported that the survival rates of corneal grafts are 68.1% in patients with CCO.[25] Another study noted that 35% of grafts would remain clear until 10 years after the procedure.[26] Timing of second eye keratoplasty is another challenge, as close intervals between surgeries can support favorable visual outcomes, reduce the risk of blindness, and maximize visual potential.[27] In our patient who presented with bilateral corneal opacities, early intervention is crucial to prevent blindness. However, given the patient's age, the risk of graft survival poses a significant concern, as reflected in previous studies.

Prior graft failures negatively impact subsequent transplant survival.[27] According to Dana, *et al*., only 19% of the 27 eyes that received a second transplant could preserve complete clarity, and none of the six eyes that received a third graft achieved this outcome.[19] Yang, *et al*., further noted that less than 10% of second or subsequent grafts would survive for three years.[27] Aphakia or pseudophakia, corneal neovascularization before transplantation, inflammation, a history of prior eye surgery, a post-graft surgical procedure, and one or more rejection episodes are risk factors for graft failure. Adherence to follow-up appointments and post-operative care is crucial for graft survival and visual rehabilitation.[21,22] Unfortunately, the patient's non-cooperation has resulted in poor adherence to medical regimens. It is shown that two weeks post-operatively, the parents only give the patient eye drops 1–2 times a day due to the child's unwillingness. This lack of compliance poses a significant risk to the long-term success of the graft. It highlights the importance of education for the family regarding the importance of adhering to the medical regimens and follow-up care.

CONCLUSION

A comprehensive workup for patients with CCO, including detailed history taking and comprehensive anterior and posterior ocular examination, is crucial for diagnosing this condition. Keratoplasty offers a viable option to restore corneal clarity and improve vision. Early surgical intervention and diligent post-operative care can significantly enhance visual outcomes and patients' overall quality of life. However, the risks and challenges associated with pediatric keratoplasty necessitate careful patient selection and comprehensive follow-up care to ensure the best possible results.

REFERENCES:

1. Shigeyasu C, Yamada M, Mizuno Y, Yokoi T, Nishina S, Azuma N. Clinical features of anterior segment dysgenesis associated with congenital corneal opacities. Cornea 2012;31:293–8. doi: 10.1097/ICO.0b013e31820cd2ab.
2. Karadag R, Rapuano CJ, Hammersmith KM, Nagra PK. Causes of congenital corneal opacities and their management in a tertiary care center. Arq Bras Oftalmol. 2020;83:98–102. doi: 10.5935/0004-2749.20200023.
3. Yulia DE, Putri FM, Soeharto DA. Clinical profile of Indonesian children with anterior segment dysgenesis as a contributor for childhood blindness. Clin Epidemiol Glob Health. 2023;20:2213–3984. https://doi.org/10.1016/j.cegh.2023.101258.
4. Rezende RA, Uchoa UB, Uchoa R, Rapuano CJ, Laibson PR, Cohen EJ. Congenital corneal opacities in a cornea referral practice. Cornea. 2004;23:565–70. doi: 10.1097/01.ico.0000126317.90271.d8.
5. Borik K, Mohney BG, Hodge D, Reynolds MM. Birth prevalence and characteristics of congenital corneal opacities. Eur J Ophthalmol. 2024;34:734–8. doi: 10.1177/11206721231202900.
6. Rajagopal RN, Fernandes M. Peters anomaly: novel non-invasive alternatives to penetrating keratoplasty. Semin Ophthalmol. 2023;38:275–82. doi: 10.1080/08820538.2023.2176238.


7. American Academy of Ophthalmology. Pediatric ophthalmology and strabismus. In: Khan A, Chang TC, El-Dairi MA, Lee KA, Utz VM, Mireskandari K, et al., editors. 2022–2023 Basic and clinical science course. San Fransisco (CA): American Academy of Ophthalmology; 2022.
8. Congenital corneal opacities - Asia Pacific [Internet]. San Fransisco (CA): American Academy of Ophthalmology; 2015 [cited 2024 Oct 1]. Available from: https://www.aao.org/education/topic-detail/congenital-corneal-opacities-asia-pacific.
9. Katzman LR, Reiser BJ. Pediatric corneal opacities [Internet]. San Fransisco (CA): American Academy of Ophthalmology; 2016 [cited 2024 Oct 1]. Available from: https://www.aao.org/education/disease-review/pediatric-corneal-opacities.
10. Kusumesh R, Vanathi M. Graft rejection in pediatric penetrating keratoplasty: clinical features and outcomes. Oman J Ophthalmol. 2015 Jan–Apr;8(1):33–7. doi: 10.4103/0974-620X.149862.
11. Abukahel A, Aldiwanie AS, Alryalat SA, Gharaibeh AM. Indications and outcomes of pediatric penetrating keratoplasty: a retrospective observational study. Med Hypothesis Discov Innov Ophthalmol. 2022 Apr 1;11(1):27–33. doi: 10.51329/mehdiophthal1442.
12. Shi W, Jin H, Li S, Liu M, Xie L. Indications of paediatric keratoplasty in north China. Clin Exp Ophthalmol. 2007;35:724–7. doi: 10.1111/j.1442-9071.2007.01618.x.
13. Chang KC, Kwon JW, Han YK, Wee WR, Lee JH. The epidemiology of cosmetic treatments for corneal opacities in a Korean population. Korean J Ophthalmol. 2010;24:148–54. doi: 10.3341/kjo.2010.24.3.148.
14. Patel HY, Ormonde S, Brookes NH, Moffatt LS, McGhee CN. The indications and outcome of paediatric corneal transplantation in New Zealand: 1991–2003. Br J Ophthalmol. 2005;89:404–8. doi: 10.1136/bjo.2004.053116.
15. Michaeli A, Markovich A, Rootman DS. Corneal transplants for the treatment of congenital corneal opacities. J Pediatr Ophthalmol Strabismus. 2005;42:34–44. doi: 10.3928/01913913-20050101-05.
16. Miao S, Lin Q, Liu Y, Song YW, Zhang YN, Pan ZQ. Clinicopathologic features and treatment characteristics of congenital corneal opacity infants and children aged 3 years or less: a retrospective single institution analysis. Med Princ and Pract. 2019;29:18. doi: 10.1159/000501763.
17. Belayneh YM, Amberbir G, Agalu A. A prospective observational study of drug therapy problems in medical ward of a referral hospital in northeast Ethiopia. BMC Health Serv Res. 2018;18:1–7. doi: 10.1186/s12913-018-3612-x.
18. Huang C, O'Hara M, Mannis MJ. Primary pediatric keratoplasty: indications and outcomes. Cornea. 2009;28:1003–8. doi: 10.1097/ICO.0b013e3181a186c0.
19. Dana MR, Moyes AL, Gomes JA, Rosheim KM, Schaumberg DA, Laibson PR, et al. The indications for and outcome in pediatric keratoplasty. a multicenter study. Ophthalmology. 1995;102:1129–38. doi: 10.1016/s0161-6420(95)30900-1.
20. Mun-Wei L, Said HM, Punitan R, Ibrahim M, Shatriah I. Indications, clinical outcomes, and survival rate of pediatric penetrating keratoplasty in suburban Malaysia: a 10-year experience. Cureus. 2018;10:e3744. doi: 10.7759/cureus.3744.
21. Gurnani B, Kaur K, Chaudhary S, Kaur RP, Nayak S, Mishra D, et al. Pediatric corneal transplantation: techniques, challenges, and outcomes. Ther Adv Ophthalmol. 2024;16:25158414241237906. doi: 10.1177/25158414241237906.
22. Trief D, Marquezan MC, Rapuano CJ, Prescott CR. Pediatric corneal transplants. Curr Opin Ophthalmol. 2017;28:477–84. doi: 10.1097/ICU.0000000000000393.
23. Lowe MT, Keane MC, Coster DJ, Williams KA. The outcome of corneal transplantation in infants, children, and adolescents. Ophthalmology. 2011;118:492–7. doi: 10.1016/j.ophtha.2010.07.006.
24. Karadag R, Chan TC, Azari AA, Nagra PK, Hammersmith KM, Rapuano CJ. Survival of primary penetrating keratoplasty in children. Am J Ophthalmol. 2016;171:95–100. doi: 10.1016/j.ajo.2016.08.031.
25. Zhang Y, Liu Y, Liang Q, Miao S, Lin Q, Zhang J, et al. Indications and outcomes of penetrating keratoplasty in infants and children of Beijing, China. Cornea. 2018;37:1243–8. doi: 10.1097/ICO.0000000000001695.
26. Lin Q, Shi W, Miao S, Zhang Y, Li L, Pan Z. Visual outcomes and prognostic factors of successful penetrating keratoplasty in 0- to 7-year-old children with congenital corneal opacities. Cornea. 2018;37:1237–42. doi: 10.1097/ICO.0000000000001689.
27. Yang LL, Lambert SR, Drews-Botsch C, Stulting RD. Long-term visual outcome of penetrating keratoplasty in infants and children with peters anomaly. J AAPOS. 2009;13:175–80. doi: 10.1016/j.jaapos.2008.10.007.