Original Article

Indications and outcomes of pediatric penetrating keratoplasty: A retrospective observational study

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ABSTRACT

Background: Pediatric corneal transplantation can be indicated in congenital and acquired conditions. Challenges include preoperative evaluation, multiple intraoperative obstacles, and postoperative problems in follow-up and management. This study was aimed at identifying the indications and clinical outcomes of pediatric penetrating keratoplasty (PKP) in Jordan.

Methods: This retrospective cohort study was conducted in Amman, Jordan. Using the hospital's electronic database, all medical records of patients aged < 18 years who underwent PKP between January 2004 and October 2019 were reviewed. Preoperative evaluations included best-corrected distance visual acuity (BCDVA) and anterior and posterior segment examinations. Postoperative complications, BCDVA, and graft survival were examined 1 year postoperatively.

Results: A total of 149 cases of pediatric PKP were performed on 141 eyes of 118 patients with an age mean ± standard deviation (SD) of 11.44 ± 4.97 years at the time of surgery. Acquired non-traumatic corneal pathologies accounted for 65.8% of indications for PKP. The most frequent indication was advanced keratoconus (55.7%). Preoperative and 1-year postoperative BCDVAs significantly differed ($P < 0.001$), with 111 (74.5%) patients showing improved BCDVA, 12 (8.05%) patients showing worsened BCDVA, and 26 (17.45%) patients showing no change in BCDVA. The overall 1-year graft survival rate was 80.54%.

Conclusions: This was the largest study in Jordan involving pediatric patients who underwent PKP for various indications, showing a significant improvement in BCDVA, with a high survival rate at 1 year. Future studies with longer follow-up periods could provide stronger evidence for surgical outcomes and graft survival. Further, the option of lamellar keratoplasty in the pediatric age group should be assessed.

KEY WORDS

pediatrics, penetrating keratoplasty, congenital, acquired, traumatic injuries, corneal grafting, keratoconus, visual acuities

INTRODUCTION

Pediatric penetrating keratoplasty (PKP) is defined as full-thickness corneal transplantation in patients younger than 18 years of age. It is rarely performed and has a high rate of graft failure and poor visual outcomes [1]. However, it remains the gold standard treatment modality to improve visual acuity, retain structural integrity, and avoid deprivation amblyopia [2-4]. PKP can be indicated in congenital and acquired conditions, with acquired conditions being traumatic or non-traumatic [5].

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How to cite this article: 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 Spring; 11(1): 27-33. https://doi.org/10.51329/mehdiophthal1442

Received: 11 March 2022; Accepted: 01 April 2022

The practice of PKP differs between developed and developing countries. For instance, the most common indications for PKP are trauma and infection in developing countries and keratoconus and congenital corneal opacities in developed countries [5-7]. Challenges in pediatric PKP include difficult preoperative evaluation; multiple intraoperative obstacles, such as a small eye size, less scleral rigidity, and positive posterior vitreous pressure; and several challenges in post-operative follow-up and management [1, 8, 9]. Nevertheless, the improved understanding of intraoperative and postoperative complications and technologic advancements have led to an increased rate of successful pediatric PKP and decreased the age at which pediatric PKP can be performed [2].

Data on pediatric PKP in the Middle East are limited. This study was aimed at identifying the indications and clinical outcomes of pediatric PKP in Jordan.

METHODS

This retrospective cohort study was conducted at the Jordan University Hospital (JUH), a tertiary medical center in Amman, the capital of Jordan, from January 2004 to October 2019. We investigated the indications and clinical outcomes of pediatric PKP at JUH over the 15-year study period. The institutional review board of the Faculty of Medicine at the University of Jordan approved the study protocol (approval number 16/204). The requirement for obtaining informed consent was waived owing to the retrospective nature of the study.

Using the hospital's electronic database, the medical records of all pediatric patients who underwent PKP between January 2004 and October 2019 were retrieved. Inclusion criteria were age < 18 years and a minimum follow-up after PKP of 1 year.

Five examiners preoperatively examined the patients. Best-corrected distance visual acuity (BCDVA) examined using a Snellen chart (automatic chart projector; TCP-4042; Tomey Co; Nagoya, Japan). A slit lamp (Slit-lamp, TSL-800H, Tomey Corp., Japan) was used to evaluate the anterior and posterior segments in cooperative children; however, examination under anesthesia was performed for younger children. Intraocular pressure was measured using the Goldmann applanation tonometer (AT900, Haag-Streit, Koeniz, Switzerland) or Tono-Pen XL (Medtronic Solan, Jacksonville, FL, USA). B-scan ultrasonography (EZ-Scan, A/B 5500 plus, Sonomed-USA) was used to evaluate the posterior segment in patients with diffuse severe corneal opacity.

Five surgeons performed all surgeries under general anesthesia. Donor corneas were imported from the Jordan Eye Bank, where they had been screened for infectious agents and endothelial quality. The trephination diameters of the donor graft and recipient bed were 5.5–8.75 and 5.0–8.5 mm, respectively. Interrupted 10-0 nylon sutures were placed in 146 grafts, and the number of stitches ranged from 10 to 23. Continuous sutures were placed in three grafts. Additional procedures, such as intraocular lens (IOL) implantation, IOL removal, anterior vitrectomy, and glaucoma drainage device insertion, were simultaneously performed in some patients. The triple procedure comprised PKP, cataract extraction, and IOL implantation.

Routine postoperative medical therapy with topical antibiotics included ofloxacin 0.3% (Oflox Allergan, Westport, Ireland) four times a day, topical prednisolone acetate suspension 1% (Pred Forte Allergan, Westport, Ireland) every 2 h, and tobramycin and dexamethasone eye ointment (TobraDex, Alcon, Puurs, Belgium) every night for a few weeks. Topical prednisolone drops were tapered in dose gradually over 6 months and then changed to fluorometholone 0.1% eye drops (FML; Allergan, Westport, Ireland), which was continued until 12 months postoperatively. Postoperative examinations were performed on the postoperative day 1, weekly for 1 month, biweekly for the next 2 months, and monthly thereafter. All sutures were routinely removed within 6 months in children younger than 5 years and 1 year in those older than 5 years. Selective suture removal was performed for suture-related problems, when indicated.

We recorded patient age at the time of surgery, sex, and surgical indication. Corneal diseases indicated for corneal transplantation were classified into congenital, acquired traumatic, and acquired non-traumatic diseases [5]. The term "PKP" was used when PKP was performed for optical correction; however, the term "tectonic graft" was used when grafts were placed to restore the structural integrity of the eye. Primary graft failure was diagnosed when graft edema persisted beyond the immediate postoperative period [10]. Graft rejection was diagnosed when grafts showed specific immune-mediated clinical signs involving any layer of the corneal graft after being clear for at least 2 weeks postoperatively [9]. Reversible graft rejection was diagnosed when the graft responded to topical steroid treatment and retained clearance, whereas irreversible rejection was diagnosed when the rejection episode leads to graft failure despite intensive treatment [11]. The survival rate was determined by the percentage of keratoplasties that survived (clear grafts) 1 year postoperatively. Postoperative complications, BCDVA, and graft survival at 1 year were also documented. Visual acuity in older children was measured using the Snellen chart and recorded using the decimal notation system. While for younger children who had inadequate verbal skills to achieve accurate visual acuity, the ability to fixate and follow targets and counting fingers were noted.

We converted counting fingers, hand motion, light perception, and no light perception to 0.014, 0.005, 0.0016, and 0.0013, respectively [12]. For a more convenient visual outcome analysis in nonverbal children, visual acuity was measured using fixation grades. Considering the inconclusive evidence for converting such grades into decimal visual acuity [13], we adopted the following approach: uncentral, unsteady, and unmaintained (UCUSUM) equal to light perception; central, unsteady, and unmaintained (CUSUM) equal to hand motion; central, steady, and unmaintained (CSUM) equal to counting fingers; and central, steady, and maintained (CSM) equal to 0.05. This conversion approach was based on the observation that a patient is expected to improve at least one step in the next visual acuity grading after PKP.

Data were analyzed using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, N.Y., USA). Continuous variables, such as age, are expressed as mean ± standard deviation (SD). Nominal variable, such as sex, are expressed as count (frequency). The independent sample *t*-test was performed to analyze the mean age difference between boys and girls. Following normality assumption, as assessed by a bar graph, the Wilcoxon signed-rank test was used to analyze the difference between preoperative and 1-year postoperative BCDVAs. "Positive differences" imply that visual acuity improved; "negative differences" imply that visual acuity worsened; and "ties" imply that visual acuity remained unchanged.

To analyze the factors affecting the change in BCDVA over 1 year, we calculated the changes in visual acuity (1-year BCDVA – preoperative BCDVA) and used the one-way analysis of variance to analyze the difference in visual acuity change with sex, indication, and surgery type. Pearson's correlation was used to determine the correlation of changes in BCDVA with age and baseline visual acuity. $P < 0.05$ was set as statistical significance.

RESULTS

A total of 149 pediatric PKPs were performed on 141 eyes of 118 patients with an age mean ± SD of 11.44 ± 4.97 years at the time of surgery. Twenty-two patients underwent bilateral PKP, while the rest underwent unilateral PKP. The mean postoperative follow-up period was 18 months (range, 6–36 months). Grafts were placed in 91 (61.1%) boys, with an age mean ± SD of 11.76 ± 4.68 years, and 58 (38.9%) girls with an age mean ± SD of 10.88 ± 5.39 years, showing no significant difference ($P = 0.297$).

Patients were divided into three categories based on age at the time of surgery: infants, ≤ 5 years (n = 24 [16.1%]); children, 6–10 years (n = 31 [20.8%]); and adolescents, 11–17 years (n = 94 [63.1%]).

The conditions indicated for pediatric PKP were classified into congenital, acquired non-traumatic, acquired traumatic, and regraft groups. The acquired non-traumatic group included 98 (65.8%) patients. The most frequent indication was advanced keratoconus (55.7%). Table 1 presents the characteristics of the included cases.

Preoperative and 1-year postoperative BCDVAs differed significantly ($P < 0.001$), with 111 (74.5%) patients showing positive differences, 12 (8.05%) patients showing negative differences, and 26 (17.45%) patients showing ties. Regarding factors affecting the change in visual acuity, the indication was a significant ($P < 0.001$), with the improvement being the highest for advanced keratoconus (0.3228) and the least for bullous keratopathy (-0.0003; Table 2).

PKP was performed to improve visual acuity in 147 (98.66%) cases. However, in two (1.34%) cases, it was performed to restore the corneal structural integrity (tectonic grafts), which had been disrupted by mechanical trauma in one case and perforated infectious keratitis in the other case (Table 3). We found a significantly greater improvement in visual acuity when PKP was performed alone ($P = 0.003$) compared to triple and other combined procedures. No significant differences were found in terms of sex ($P = 0.307$).

The age and change in visual acuity showed a positive correlation (r = 0.444; $P < 0.001$), but baseline and 1-year visual acuities showed no correlation (r = - 0.12; $P = 0.065$).

The overall graft survival rate at 1 year was 80.54%. Graft failure occurred in 29 (19.46%) cases. Causes of graft failure were primary in 15 (51.72%) cases, irreversible rejection in 10 (34.48%) cases, uncontrolled glaucoma in three (10.34%) cases, and infection in one (3.45%) case. The graft failure was not significantly different between age categories ($P > 0.05$). Of the 29 failed grafts, nine were in infants, ten in children, and ten in adolescents.

Major postoperative complications occurred in 95 (63.76%) grafts. The loose suture was the most common complication, reported in 47 (31.54%) cases (Table 4). All patients required an additional procedure to remove loose stitches. This was accomplished in the operating room for infants and children and in the clinic for cooperative adolescents. Corneal graft rejection was the second most common complication, documented in 23 (15.4%) grafts (Table 4). Reversible graft rejection occurred in 14 grafts and was successfully treated with a topical corticosteroid. Irreversible rejection with secondary graft failure was reported in nine grafts.

Table 1. Characteristics of study participants

Variable		Mean ± SD or n (%)
Age (y)		11.44 ± 4.96
Sex (Male /Female)		91 (61.1) / 58 (38.9)
Indications	**Acquired non-traumatic**	**98 (65.8)**
	Advanced keratoconus	83 (55.7)
	Keratitis scar	10 (6.7)
	Corneal dystrophy (Granular type)	2 (1.3)
	Keratoglobus	2 (1.3
	Bullous keratopathy	1 (0.7)
	Acquired traumatic	**24 (16.1)**
	Traumatic opacity	23 (15.4)
	Chemical burn	1 (0.7)
	Congenital	**17 (11.4)**
	Congenital glaucoma	11 (7.4)
	Congenital corneal opacity	6 (4.0)
	Regraft	**10 (6.7)**
Surgery	**PKP**	**135 (90.6)**
	Combined procedures	**12 (8.1)**
	Triple procedure	7 (4.7)
	PKP with IOL implantation	1 (0.7)
	PKP with IOL removal	1 (0.7)
	Triple with GDD insertion	1 (0.7)
	PKP with anterior vitrectomy	2 (1.3)
	Tectonic	**2 (1.3)**
BCDVA Preoperative		0.0329 ± 0.0503
BCDVA at 1 year postoperative		0.2381 ± 0.2301

Abbreviations: SD, standard deviation; n, number; %, percentage; y, year; PKP, penetrating keratoplasty; The triple procedure, Triple procedure includes penetrating keratoplasty, cataract extraction, and intraocular lens implantation; IOL, Intraocular lens; GDD, Glaucoma drainage device; BCDVA, best-corrected distance visual acuity.

Table 2. Difference between the change in preoperative and 1-year postoperative best-corrected distance visual acuity among different indications for pediatric penetrating keratoplasty

Indication (n)		Mean ± SD	95% CI for Mean
Acquired non-traumatic	Advanced Keratoconus (83)	0.3228 ± 0.2024	0.2786–0.3670
	Keratitis scar (10)	0.1029 ± 0.1684	- 0.0176–0.2234
	Granular Corneal dystrophy (2)	0.3680 ± 0.0255	0.1393–0.5967
	Keratoglobus (2)	0.2000 ± 0.1414	- 1.0706–1.4706
	Bullous keratopathy (1)	- 0.0003 ± -	-
Acquired traumatic	Traumatic opacity (23)	0.0660 ± 0.1280	0.0106–0.1213
	Chemical burn (1)	0.0000 ± -	-
Congenital	Congenital glaucoma (11)	0.0072 ± 0.0110	- 0.0002–0.0145
	Congenital corneal opacity (6)	0.0020 ± 0.0037	- 0.0019–0.0059
Regraft	Failed previous graft (10)	0.0014 ± 0.0059	- 0.0028–0.0057
Total (149)		0.2052 ± 0.2163	0.1702–0.2402

Abbreviations: PKP, penetrating keratoplasty; n, number; SD, standard deviation; CI, confidence interval.

Table 3. Difference between the change in preoperative and 1-year postoperative best-corrected distance visual acuity among different types of surgeries

Surgery (n)	Mean ± SD	95% CI for Mean
Optical PKP (135)	0.2251 ± 0.2149	0.1887–0.2616
Combined procedures (12)	0.0116 ± 0.0295	- 0.0095–0.0328
Tectonic PKP (2)	0.0000 ± 0.0000	0.0000–0.0000
Total (149)	0.2077 ± 0.2143	0.1728–0.2425

Abbreviations: n, number; SD, standard deviation; CI, confidence interval; PKP, penetrating keratoplasty. Note: Combined procedures included the triple procedure, triple procedure with glaucoma drainage device insertion, penetrating keratoplasty (PKP) with intraocular lens insertion, intraocular lens removal, and PKP with anterior vitrectomy; Optical PKP means PKP for optical correction; Tectonic PKP means PKP to restore structural integrity of the eye.

Table 4. Frequency of pediatric penetrating keratoplasty complications after 1 year

Type of complication	n (%)
Loose suture	47 (31.5)
Rejection	23 (15.4)
Neovascularization	17 (11.4)
Primary graft failure	17 (11.4)
Cataract	8 (5.4)
High intraocular pressure	8 (5.4)
Keratitis	7 (4.7)
Traumatic dehiscence	6 (4.0)
Persistent epithelial defect	5 (3.4)
Peripheral anterior synechiae	5 (3.4)
Squint	3 (2.0)
Phthisis	2 (1.3)
Iris prolapse	2 (1.3)
Wound leak	1 (0.7)
Iris cyst	1 (0.7)
Retinal detachment	1 (0.7)
Recurrence of dystrophy	1 (0.7)
Band keratopathy	1 (0.7)
Exposure keratopathy	1 (0.7)

Abbreviations: SD, standard deviation; n, number; %, percentage.

DISCUSSION

Our study included 149 PKPs performed in children with a mean age of 11.44 years at the time of surgery. Acquired non-traumatic corneal pathology was the indication in 65.8% of cases. The most frequent indication was advanced keratoconus (55.7%). The visual acuity improved significantly, with a high survival rate at 1 year.

Corneal disorders are a leading cause of visual impairment in children. Although pediatric PKP is a challenging procedure, it is essential to treat vision-threatening corneal pathologies, particularly those found in the early stages of visual system development [14, 15]. This retrospective study described the indications and clinical outcomes of pediatric PKP in JUH over a 15-year study period. To the best of our knowledge, studies on pediatric PKP are scarce in the Middle East [16, 17]. Various indications for PKP have been reported worldwide. Our results showed that more than half of the corneal grafts were placed to treat advanced keratoconus (55.7%), which belongs to the acquired non-traumatic group. Similar results were reported from Tunisia [1], Mexico [3], New Zealand [5], Australia [18], and Denmark [10].

Shi et al. reported that corneal opacity after mechanical trauma was the most common indication for pediatric PKP in China [4]. In our study, traumatic corneal opacity was the second most common indication (n = 23, 15.4%). In India, scarring after keratitis (n = 22, 33.4%) was reported as the most common indication for pediatric PKP [19]; however, it was the indication in only a few cases in our study. Although cases of congenital corneal opacities were fewer in our study (11.4%), other authors reported them as a major indication for pediatric PKP [8, 20].

Graft survival and improvement in visual acuity reflect the success of corneal transplantation [7]. Similar to other studies [1, 21], we found a significant visual acuity improvement in 74.5% of grafts.

Some studies have reported a correlation between the indication for corneal grafting and visual acuity improvement. Patel et al. reported significantly improved visual acuity in acquired conditions than in congenital conditions [5], consistent with our study, in which better acuities were noted in patients grafted for advanced keratoconus. Amblyopia in children with congenital opacities was responsible for the poor visual acuity after corneal grafting [6, 22]. Congenital corneal opacities were seen in only six cases in our study, which could skew the result of better visual outcomes.

We found a significant correlation between age and changes in visual acuity. Older children had better visual acuity compared to younger children, consistent with the results of Lowe et al. [18]. While Lin et al. reported quite contrary results, who found no significant association between age at the time of PKP and visual outcomes [22].

Potential factors affecting corneal graft survival include age at the time of surgery and surgical procedures performed in addition to PKP. Although we found no correlation between the age and graft failure, previous studies reported that older children have a better prognosis [7, 9, 21].

The effect of combined procedures on graft failure is another factor. Some studies reported a low survival rate in grafts performed with additional procedures [20, 21, 23]. The relationship between combined procedures and graft survival was inconclusive in our study, attributable to the fact that additional procedures were performed in only 12 (8.1%) cases. We believe that this difference in pediatric PKP outcomes is due to the heterogeneity of the samples across studies. Our sample had a higher frequency of adolescents and acquired non-traumatic cases, which may cause bias in the result of better outcomes. Major postoperative complications were reported in 63.76% of grafts. The most frequent one was loose sutures, reported in 31.54% of grafts.

Younger patients have a more active immune system, rendering them more prone to graft rejection [3]. In a previous study, graft rejection was the most common complication, documented in 12.1% of cases [19]. In our study, it was the second most common complication (n = 23, 15.4%). Limaiem et al. reported a higher rate of graft rejection at 31% of cases [1].

To minimize the risk of complications of full-thickness keratoplasty, the role of lamellar keratoplasty has been described [21]; however, all of our grafts were full-thickness. Lamellar keratoplasty is gaining popularity in adults but is less frequently performed in children [24].

Our study provided valuable information about pediatric PKP in Jordan. A key strength of the present study is the sample size, while the limitations of this study include the retrospective design and short-term follow-up. Future prospective studies with a longer follow-up period should verify the surgical outcomes and graft survival rates noted in this study. Moreover, future studies should assess the option of lamellar keratoplasty in children.

CONCLUSIONS

In this large-scale study on indications of pediatric PKP in Jordan, BCDVA showed improvement, with a high survival rate at 1 year. Available data on PKP in Middle Eastern countries are limited. Therefore, this study could enrich pediatric PKP data in this region. Future studies with longer follow-up periods could provide stronger evidence for surgical outcomes and graft survival. Further, the option of lamellar keratoplasty in the pediatric age group should be assessed.

ETHICAL DECLARATIONS

Ethical approval: The institutional review board of the Faculty of Medicine at the University of Jordan approved the study protocol (approval number 16/204). The requirement for obtaining informed consent was waived owing to the retrospective nature of the study.
Conflict of interest: None.

FUNDING

None.

ACKNOWLEDGEMENTS

None.

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