

Complications in deep anterior lamellar keratoplasty – A retrospective interventional analysis in a large series

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Purpose: To analyze the complications in patients managed with deep anterior lamellar keratoplasty (DALK) for diseases of the anterior corneal stroma. **Methods:** This is a retrospective analysis of all the patients who underwent DALK in a tertiary care center in South India from 2010 to 2020. A total of 474 eyes in 373 patients were included in the study. Patients who underwent DALK for advanced keratoconus, keratoconus with Bowman's membrane scar, healed hydrops, macular corneal opacity, macular corneal dystrophy, granular corneal dystrophy, spheroidal degeneration, pellucid marginal degeneration, post-laser-assisted *in situ* keratomileusis ectasia, descemetocoele, post-collagen cross-linking aborted melt and dense scar, and post-radial keratotomy were included in the study. The patients were followed up for 17.2 +/- 9.2 months (1–9 years). **Results:** Complications noted in the surgery were intra-operatively Descemet's membrane perforation in 31 eyes (6.54%), post-operatively secondary glaucoma in 16 eyes (3.37%), cataract in seven eyes (1.47%), suture-related complications in five eyes (1.05%), graft rejection in three eyes (0.63%), traumatic dehiscence in two eyes (0.42%), filamentary keratitis in two eyes (0.42%), interface infiltrate in one eye (0.21%), and recurrence of disease in four eyes (7.14%) out of 57 eyes with corneal dystrophy. **Conclusion:** DALK as an alternative to penetrating keratoplasty for anterior corneal stromal diseases. It has become an automatic choice for diseases of the anterior cornea requiring keratoplasty. Complications can occur at any stage of surgery; however, if identified and managed early, they can result in optimal outcome.

Key words: Deep anterior lamellar keratoplasty, Descemet's membrane perforation, double anterior chamber, graft rejection, interface infectious keratitis

Deep anterior lamellar keratoplasty (DALK) is performed in diseases of the anterior corneal stroma in which the pathologic corneal stroma is replaced with donor graft sparing the corneal endothelium eliminating endothelial graft rejection and reduced rates of endothelial cell count. It overcomes multiple complications associated with penetrating keratoplasty being an open globe surgery, complications such as expulsive hemorrhage, endophthalmitis, and so on. The most commonly performed surgical technique is the Anwar big bubble technique invented in 1974;^[1] this technique has multiple benefits over manual stromal dissection. Indications for DALK are advanced keratoconus, pellucid marginal degeneration, progressive post-laser-assisted *in situ* keratomileusis (LASIK) ectasia, hereditary stromal dystrophies, corneal stromal scars, infectious keratitis, and tectonic indications. Contraindications include a dysfunctional endothelium and deep scars involving Descemet's membrane in the visual axis.

The purpose of this article is to evaluate the intra-operative and post-operative complications related to DALK.

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Methods

The patients who had undergone DALK in a tertiary eye care hospital in South India from the period of 2010–2020 were retrospectively analyzed for complications after surgery. A total of 474 eyes in 373 patients were included in the study. Patients who had undergone DALK for a) keratoconus, b) macular corneal opacity c) post-collagen cross-linking aborted corneal melt, d) hereditary stromal dystrophies, e) corneal degeneration, f) pellucid marginal degeneration, g) post-LASIK ectasia, h) descemetocoele, and i) post-radial keratectomy were included in the study. Table 1 shows indications for DALK in our study.

Pre-operative data collection included age, sex, visual acuity, ocular examination, surgical history, and anterior segment optical coherence tomography. Post-operatively, the type of procedure, visual acuity, complications, and duration of follow-up were noted. Based on the type of corneal stromal disease, an appropriate surgical technique of performing DALK was opted.

Most of the cases were performed under peri-bulbar anesthesia using 5 ml 2% lignocaine and 5 ml 0.75% bupivacaine except a few, which needed surgery under general anesthesia.

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For patients with stromal diseases not involving Descemet's membrane, the big bubble technique invented by Anwar and Teichmann was performed, in which after approximately 70–80% of host corneal trephination, a 26-gauge needle attached to a sterile air-filled 5 cc syringe is introduced into the deep stroma with the bevel facing downward toward the central cornea. Air is then gently injected, which forms a round, well-demarcated big bubble extending to the borders or beyond borders of trephination. Trephination was performed of the same size in the donor and recipient corneas in keratoconus patients, whereas a discrepancy of 0.25 mm was implied in all the other cases. A deeper trephination is performed in patients with advanced keratoconus having anterior and mid-stromal scars. Post this, de-bulking of the anterior 2/3rd of the stroma is performed using a crescent blade and Lim's forceps. Then, with no. 11 blade, a central bold nick is given to collapse the bubble, post which a viscoelastic is injected through the nick incision to keep the Descemet's away from all the manipulations. The posterior lamella was then divided into 4–5 segments and excised using a Vannas' scissor to explore the smooth Descemet's. The donor corneal tissue Descemet's endothelial layer is scraped off using a merocel sponge or a non-toothed forceps and is then placed over the host cornea after thorough irrigation of the host bed with saline to remove all viscoelastic substances and then secured with 16 interrupted sutures when the selected donor graft size is more than 8 mm and with 12 interrupted sutures when the donor graft size is 8 mm or less.

The manual layer-by-layer stromal dissection technique was performed in patients with healed hydrops, those with keratoconus with posterior stromal scars, those with the formation of a type 2 or type 3 bubble intra-operatively, and those with descemetocoele. Air bubble injection at a superficial layer is performed to create emphysema of the cornea, which helped in easy dissection, and subsequently stromal removal using a bevel-up crescent knife. In two eyes which showed perforation during air bubble injection, they were managed by removing the needle and introducing it at a superficial level to create stromal hydration and subsequently stromal dissection. Layer-by-layer stromal dissection and resection are repeated until the deep stromal layer or pre-descemetocoele layer is approached. Then, the donor graft is placed and secured with interrupted sutures.

Post-operatively, all the patients were started on topical antibiotics (0.5% Moxifloxacin), 4 times/day for 2 weeks, topical steroids (1% Prednisolone) 6 times/day for the first week and then tapered gradually, and preservative-free tear substitutes (0.5% carboxymethyl cellulose) for 6 weeks. The patients were followed at day 1, 2 weeks, 6 weeks, 6 months initially after the surgery, and then every 6 months thereafter. All the complications during and after surgery during the follow-up period were noted, and appropriate corrective measures were taken to address the complications. The study was approved by the institutional ethics committee and adhered to the tenets of the Declaration of Helsinki.

Results

The study included 474 eyes of 373 patients, and these patients were retrospectively analyzed. A total of 331 eyes were treated for patients with keratoconus, 35 eyes for patients with macular corneal opacity, 29 eyes for macular corneal dystrophy, 27 eyes for granular corneal dystrophy, 18 eyes for spheroidal degeneration, ten eyes for post-LASIK ectasia, seven eyes for patients who

had aborted corneal melt post-collagen cross-linking, six eyes for progressive corneal ulcer with descemetocoele, six eyes with multiple linear irregular scars post radial keratotomy, and five eyes for pellucid marginal degeneration. Out of 373 patients, 176 patients were male and 197 patients were female. The follow-up period ranged from 1 year to 9 years, with an average of 16 months. Demographic data, the number and types of anterior corneal stromal diseases included in the study, and the follow-up period are shown in Table 2.

Intra-operatively 31 (6.54%) eyes had Descemet's membrane perforation, among which 18 eyes had perforation during layer-by-layer dissection of the stroma in healed hydrops [Fig. 1], ten eyes had perforation during dissection of a type 2 bubble in macular corneal opacities, two eyes had perforation during air injection, and one eye had perforation

Table 1: Indications of DALK in our study

Indications	Number Of Eyes
Keratoconus	331 (69.83%)
Macular corneal opacity	35 (7.38%)
Macular corneal dystrophy	29 (6.11%)
Granular corneal dystrophy	27 (5.69%)
Spheroidal degeneration	18 (3.79%)
Post-LASIK ectasia	10 (2.10%)
Post-collagen cross-linking aborted corneal melt	7 (1.47%)
Descemetocoele	6 (1.26%)
Post-radial keratotomy	6 (1.26%)
Pellucid marginal degeneration	5 (1.05%)

Table 2: Demographic data of the study and follow-up period

Heading	Numbers
Number of patients	373
Total number of cases	474
Unilateral : Bilateral	272 : 101
Male : Female	176 : 197
Mean age	29 +/- 13.2 years (range 10-63 years)
Mean follow-up period	17.2 +/- 9.2 months (1-9 ears)

Table 3: List of all the complications with their respective percentages

Complications	No. of eyes (%)
Descemet's membrane perforation	31 cases (6.54%)
Increased IOP	16 eyes (3.37%)
Cataract	7 eyes (1.47%)
Recurrence of disease	4 eyes (7.14%) out of 56 eyes
Stromal graft rejection	3 eyes (0.63%)
Suture-related infiltrates	2 eyes (0.42%)
Graft dehiscence	2 eyes (0.42%)
Filamentary keratitis	2 eyes (0.42%)
Interface Vascularization	2 eyes (0.42%)
Infiltrates in the interface	1 eye (0.21%)
Suture abscess	1 eye (0.21%)

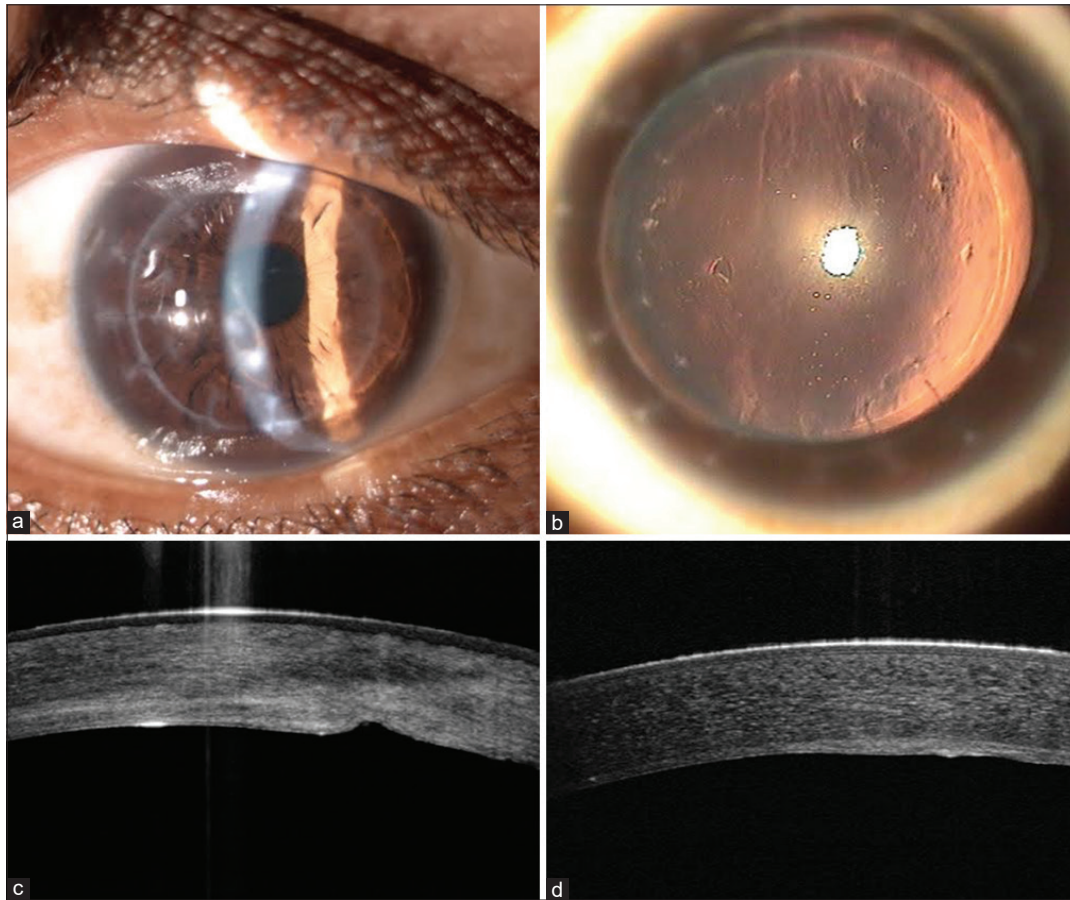


Figure 1: Intra-operative complications: (a) Outcome after macro-perforation of Descemet's membrane, (b) outcome after micro-perforation of Descemet's membrane, (c) pre-operative anterior segment optical coherence tomography picture of healed acute hydrops, and (d) post-operative picture of the same patient showing healed Descemet's perforation

while suturing of the donor graft. The following post-operative complications were noted in these 474 cases. Various causes of intra-ocular pressure (IOP) rise were noted in 16 eyes (3.37%); post-operative steroid use was induced in 11 eyes (9.09%) because of angle closure by the air bubble in the anterior chamber in four eyes (0.84%) and because of angle closure by the big bubble in the anterior chamber in one eye (0.21%). Cataract was also observed as a post-operative complication in seven eyes (1.47%). Stromal graft rejection was observed in three eyes (0.63%). Suture-related infiltrates were seen in two eyes (0.42%), and dense infiltrate in the interface was seen in one eye (0.21%). There were also uncommon complications such as graft dehiscence because of trauma in two eyes (0.42%); filamentary keratitis was observed in two eyes (0.42%); abscess related to sutures was observed in one eye (0.21%); vascularization of sutures was observed in two eyes (0.42%) with vernal keratoconjunctivitis; and hereditary corneal dystrophies, which can recur in the donor tissues, were observed in two eyes (6.8%) out of 27 eyes with granular corneal dystrophy and two eyes (7.4%) out of 29 eyes with macular corneal dystrophy [Fig. 2]. Table 3 shows the list of all the complications with their respective percentage.

The best corrected visual acuity post-operatively was in the range of 6/6 to 6/12 in 433 eyes (91.3%) and 6/18 to 6/36 in 36 eyes (7.5%), which included 12 eyes treated for macular

corneal dystrophy, eight eyes for granular corneal dystrophy, six eyes for descematocele, six eyes for amblyopia, four eyes for high astigmatism, and two eyes for macular scar. Less than 6/36 was observed in four eyes, among which one eye had traumatic aphakia, one eye had retinal detachment, one eye had neurotrophic keratitis, and one eye had abscess at the suture tract.

Discussion

DALK has been performed for anterior corneal diseases by experienced surgeons as it demands special skills with a longer learning curve. Over the period of time, the DALK procedure has been evolved for the benefit of surgeons and also to reduce the intra-operative complications associated with the conventional penetrating keratoplasty. However, multiple complications are reported intra-operatively and post-operatively in DALK and various measures are adopted to overcome these complications. Here in this article, we analyzed various complications which occur during various stages of surgery and after the surgery. Table 4 shows a comparison of incidence of complications of other studies with our study.

Descemet's membrane perforation

Descemet's membrane perforation has been reported as one of the intra-operative complications in various studies. This complication can happen during trephination, during

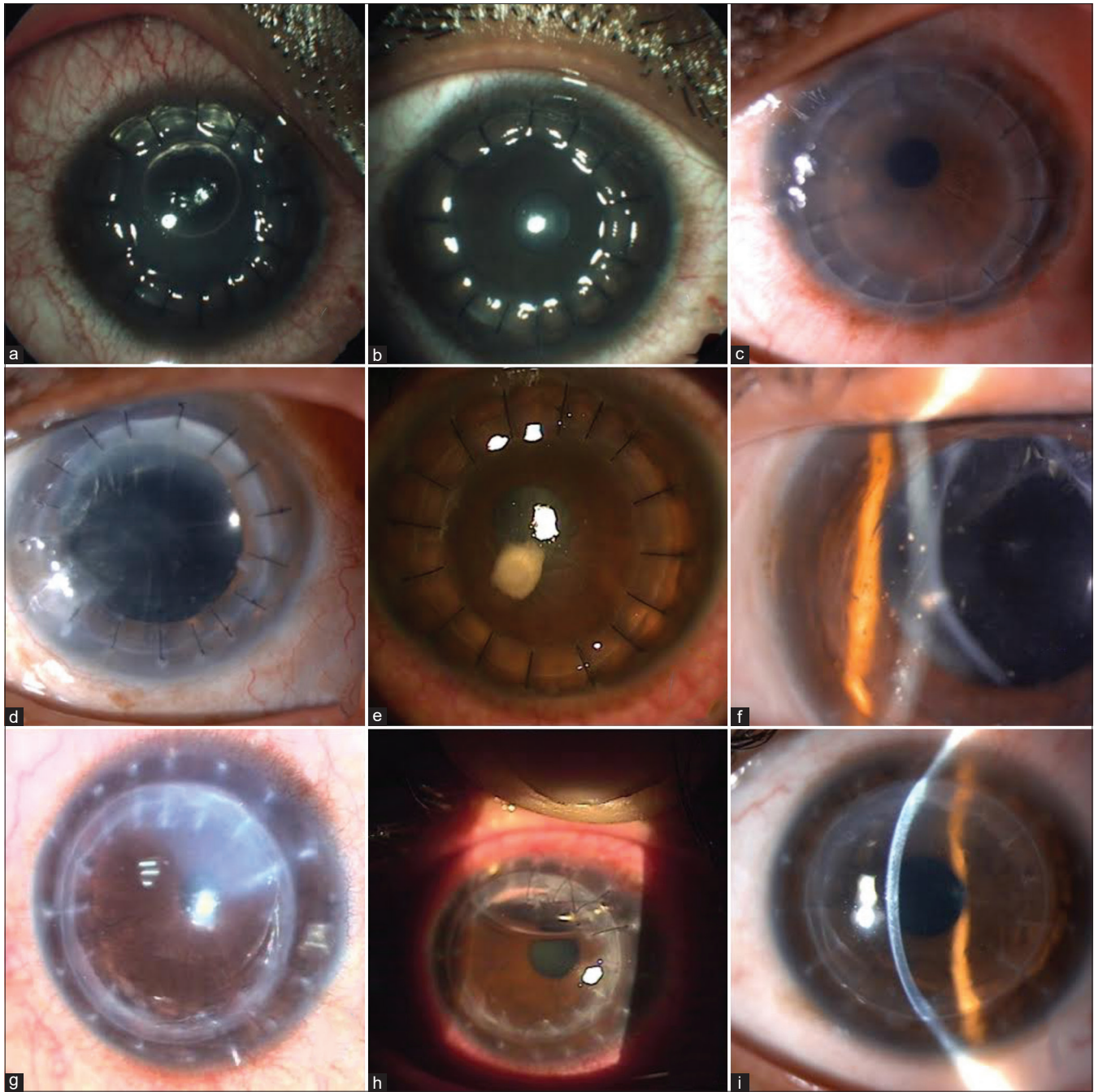


Figure 2: Slit-lamp photograph of post-operative complications showing (a) double anterior chamber, (b) post-operative picture of the same patient after management, (c) raised IOP with graft edema, (d) therapeutic DALK performed in descematocele with minimal central scarring, (e) interface infectious keratitis, (f) recurrence of granular corneal dystrophy, (g) Descemet's membrane detachment after suture removal, (h) same patient after corrective suturing of detached Descemet's membrane, and (i) stromal graft rejection

stromal air injection, during manual layer-by-layer dissection, or during suturing. In our study, perforation occurred in 31 cases (6.54%), which was observed during layer-by-layer dissection in 18 eyes (58.06%) of patients having treated for healed hydrops, two eyes (6.45%) during air bubble injection, ten eyes (32.2%) with type 2 big bubble formation, during layer-by-layer dissection, in cases of macular corneal opacity and advanced Keratoconus (KC) with deep scar, and one eye (3.22%) during suturing. Olivia S Huang et al. conducted a study showing perforation in 101 eyes (18.7%), which included

79 eyes (78.2%) with micro-perforations and 15 eyes (14.9%) with macro-perforations.^[3] Intra-operations were during deep lamellar dissection (32 cases, 31.7%), air injection (27 cases, 26.7%), and suturing (21 cases, 20.8%).^[4] Lecissotti A *et al.* conducted a study on prognosis of patients with intraoperative descemet's membrane perforation which occurred in 8 eyes (23%), in 5 eyes during manual deep dissection and in 1 eye each during trephination, suturing and while collapsing Big Bubble.^[4] A similar outcome was noted with other studies.^[5,9,10] Its management depends on the size and location of

Table 4: Comparison of DALK complications of other studies with our study

Author	No. Of eyes	Mean follow-up	Intra-operative Descemet's membrane perforation	Stromal Graft rejection	Rise in IOP	Double anterior chamber	Suture-related complications	Vascularization	Interface-related complications	Recurrence of hereditary corneal dystrophy
Our study	474	17.2 +/-9.2 months (1-9 yrs)	31 (6.54%)	3 eyes (0.63%)	16 eyes (3.37%)	3 eyes (0.63%)	2 eyes (0.42%)	2 eyes (0.42%)	1 eye (0.21%)	4 eyes (7.14%)
Saber H EI Sayed <i>et al.</i> ^[2]	47	12 months	4 (8.5%)	1 (2.1%)			11 (23.4%)	3 (6.4%)		
Olivia S Huang <i>et al.</i> ^[3]	540		101 (18.7%)							
Leccisotti A <i>et al.</i> ^[4]	35		8 (23%)							
Mohamed Hosny <i>et al.</i> ^[5]	40		9 (22.5%)							
Evan A Olson <i>et al.</i> ^[6]	22			5 (22.7%)						
Yumiko Hirayama <i>et al.</i> ^[7]	305			6 (0.01%)						
Fayyaz U Musa <i>et al.</i> ^[8]	69	54.9 months			12 (17%)					

perforation and the stage at which the perforation happened; if it happened during the initial stage of trephination, then depending upon the size of perforation, micro-perforations toward the end of dissection were continued as DALK and macro-perforations in the initial stage of dissection, especially if central, were converted to penetrating keratoplasty. When the perforation happened during layer-by-layer stromal dissection, the dissection was performed away from the perforation site, all around the perforation, first leaving a small bit of the posterior stroma above the perforation and eventually sealing it with an air bubble in the anterior chamber. Perforation which happened during the suturing technique was also managed with an air bubble in the anterior chamber. The percentage decrease in endothelial cell count was evaluated in 16 patients at the sixth post-operative week as 7.48% and at the sixth month and 1 year post-operative as 15.1%.

Graft rejection

Graft rejection is comparatively uncommon in DALK as it overcomes endothelial rejection,^[11] however, epithelial and stromal graft rejection are still bound to happen. Antigen-presenting cells should be able to reach the donor stroma through two pathways: 1) via intra-stromal recognition, that is, antigen-presenting cells could migrate into the stromal tissue via stromal fibers, or 2) via infiltrating vessels in the high-risk model.^[12] In our study, stromal graft rejection occurred in three eyes (0.63%); all three eyes had vernal kerato conjunctivitis with active inflammation, which were successfully managed with topical steroids. Stromal graft rejections can be well managed with aggressive topical steroids (prednisolone 1% hourly) as observed in many studies;^[6,7,13] also, prompt treatment avoids its long-term complications such as graft vascularization and poor visual outcomes. Its incidence can range from 1 to 29%.^[14]

Rise in intra-ocular pressure

Although studies show insignificant incidence of a rise in intra-ocular pressure (IOP), post-DALK surgery needs attention and prompt treatment to avoid its consequences. Its incidence is observed from 0 to 9%.^[15] Overall, this rise in IOP was observed in 16 eyes (3.37%) because of long-term steroid use in 11 eyes (68.75%), which was treated by regulating its dose, because air bubble injection in the anterior chamber was seen in four eyes (25%), leading to pupillary block and subsequent secondary angle closure.^[16] In one eye (6.25%), it was because of reverse pupillary block because of the big bubble. Fayyaz U Musa *et al.*^[8] conducted a study to report the incidence of raised IOP post DALK, which happened in 12 eyes (17%) out of 69 cases, and all were related to a temporary rise because of prolonged topical steroid use in the post-operative period. Multiple other studies have been documented showing raised intra-ocular pressure post DALK.^[17,18]

Double anterior chamber

This complication occurs commonly in patients with breaks in Descemet's membrane and the air bubble in the anterior chamber.^[19] In our study, three eyes (0.63%) had a double anterior chamber and were managed conservatively in two cases. The incidence of the double anterior chamber has been quiet common post DALK and is reported in multiple studies.^[20,21]

Suture-related complications

As an observation, suture-related complications such as suture loosening, vascularization, and sterile reactions and infiltrates are observed more commonly in DALK.^[19] In

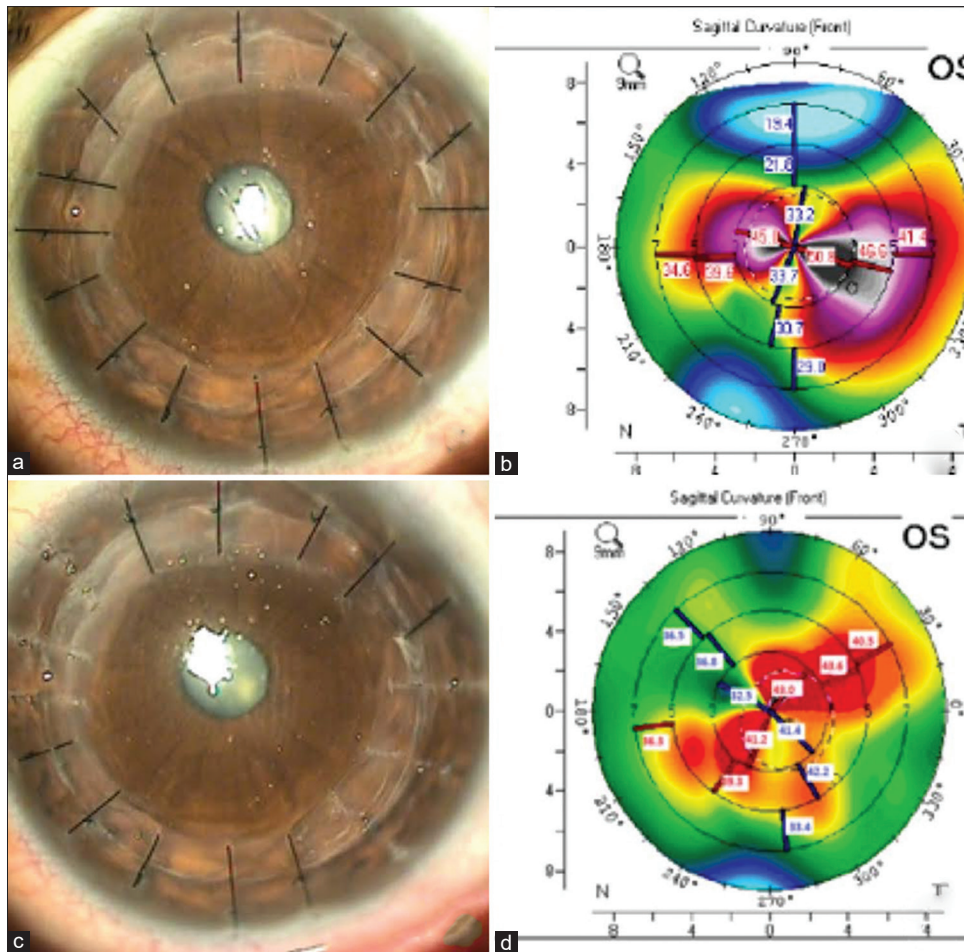


Figure 3: Astigmatism correction: (a) Slit-lamp photograph of a patient showing tight sutures at the corresponding steep axis, (b) topography of the same patient showing high astigmatism, (c) slit-lamp photo after the removal of the suture, and (d) topography showing reduction in astigmatism

our study, suture infiltrates were seen in two eyes (0.42%), suture-related vascularization observed in patients with vernal keratoconjunctivitis was seen in two eyes (0.42%), and one of the dreadful complications as suture-related abscess was observed in one eye (0.21%). El Sayed SH *et al.*^[2] study encountered loosening of the sutures in 11 cases (23.4%) and vascularization of the sutures in three cases (6.4%).

Interface-related complication

As the interface is a potential space for growth of micro-organisms, interface keratitis has been one of the intractable complications because of its location as the sample collection and drug penetration are remotely accessible. Thankfully, its incidence is very low and most commonly occurs after contamination of the donor graft and mostly with *Candida* species.^[22] In our study, it occurred only in one eye (0.21%) and was successfully managed by modified de-bulking. Kodavoor SK *et al.*^[23] also reported a case of interface fungal keratitis which was successfully managed aggressively with topical anti-fungal medication. The rate of interface keratitis caused by the fungal agent post DALK is reported as 0.052%.^[24] Multiple case reports are documented and were treated successfully.^[22,25]

Recurrence of hereditary stromal dystrophies

Until now, 18 cases of recurrence in granular corneal dystrophy have been recorded from 6 months to 8.5 months with varying patterns.^[26] In our study, two eyes (0.42%) showed its

recurrence; hence, it becomes a source of its incidence. A study conducted by Esin Sogutlu Sari *et al.*^[27] on recurrence of macular corneal dystrophy reported it as 5.7%; however, it was observed only in two eyes (0.42%) in our study. A comparative study was conducted by Kodavoor SK *et al.*^[28] between the outcomes of macular and granular corneal dystrophy, which concluded comparable results.

Astigmatism

In our study, four eyes showed significant astigmatism post-operatively, which disturbed the vision of patients, and were managed by removing selective sutures under the guidance of topography [Fig. 3]. As shown in the picture, a patient who had a refractive error of + 4.00 D spherical with -10.00 D cylinder at 10 degrees improving to 6/24 was corrected to + 1.75 D spherical with -4.00 D cylinder at 165 degrees improved to visual acuity of 6/9 on the Snellen chart after removal of sutures, which is also shown in the topography correspondingly.

Miscellaneous complications

Some uncommon complications were observed in our study, which are necessary to be reported; for example, filamentary keratitis was observed in two eyes (0.42%), and they were well managed with lubricating drops; also, traumatic dehiscence of the graft was observed in two eyes (0.42%). Traumatic dislocation was reported in one case (0.21%) which required penetrating keratoplasty on an emergency basis. Also, traumatic

aphakia, neurotrophic keratitis, and retinal detachment were observed as solitary post-operative complications. Descemet's membrane separation after suture removal was observed in one eye, and the patient was successfully managed with corrective re-suturing at the site of detachment.

Cataract

Cataract was observed in seven eyes (1.47%) post DALK, mostly steroid-induced, causing posterior sub-capsular cataract, among which three cases needed cataract surgery with intra-ocular lens implantation. A number of studies have already confirmed lesser incidence of cataract post DALK as compared to penetrating keratoplasty.^[29,30]

In our study, therapeutic DALK was performed in six eyes with descemetocele, and all had successful outcomes. A study was conducted by Hong The Nguyen *et al.*,^[31] in which therapeutic DALK was performed successfully in all 24 cases.

Conclusion

DALK as an alternative to penetrating keratoplasty for anterior corneal stromal diseases has proven to be better time and again. It has become an automatic choice for diseases of the anterior cornea requiring keratoplasty, but it is not without complications. Complications can occur at any stage of surgery; however, if identified and managed early, they can result in optimal outcome. This article compiles complications post DALK.

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Conflicts of interest

There are no conflicts of interest.

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