

## Endophthalmitis with opaque cornea managed with primary endoscopic vitrectomy and secondary keratoplasty: Presentations and outcomes

Vivek P Dave<sup>1</sup>, Rajeev R Pappuru<sup>1</sup>, Mohammad A Khader<sup>1,2</sup>, Sayan Basu<sup>3</sup>, Mudit Tyagi<sup>1</sup>, Avinash Pathengay<sup>4</sup>

**Purpose:** To describe the outcomes of endophthalmitis with opaque cornea managed with primary endoscopic vitrectomy and secondary keratoplasty. **Methods:** Retrospective consecutive interventional case series. All cases of endophthalmitis with opaque cornea which underwent endoscopic vitrectomy followed by secondary keratoplasty were analyzed. The study period was from Jan 2015 to March 2019. The outcome measures were resolution of infection, the magnitude of unnecessary keratoplasties avoided and corneal graft survival. The final anatomic and functional outcomes were reported and compared with relevant literature. **Results:** Seventy-eight eyes of 78 patients underwent endoscopic pars plana vitrectomy for endophthalmitis with the opaque cornea, of these 14 eyes of 14 patients were deemed eligible for further corneal intervention and were included in the study. The mean age at presentation was  $42.27 \pm 21.6$  years (median 36 years). Etiology-wise, eight cases (57.14%) were post-trauma, three cases (21.42%) post-keratoplasty, two cases (14.28%) were endogenous, and one case (7.14%) following corneal dermoid excision and wound melt. Culture positivity was in 5/14 (35.71%). The mean interval between endoscopic vitrectomy and keratoplasty was  $5.42 \pm 2.69$  months (median 3.5 months). The mean follow-up noted was  $20.42 \pm 11.45$  months (median 17.5 months). The infection resolved in 100% of cases. Unnecessary keratoplasties were avoided in 64/78 (82%) cases due to the primary endoscopic intervention. The favorable anatomic outcome was seen in 11/14 (78.57%) of cases and favorable functional outcome in 8/14 (57.14%) cases. **Conclusion:** Endoscopic vitrectomy allows for early intervention in endophthalmitis with the opaque cornea. This facilitates early settlement of infection, globe preservation, greater graft survival, and lesser repeat posterior segment procedures.

**Key words:** Endophthalmitis, endoscopic vitrectomy, keratoplasty

Endophthalmitis is defined as inflammation of the inner layers of the eye with exudation in the vitreous cavity resulting from intraocular colonization by microorganisms.<sup>[1]</sup> The present understanding suggests that early vitrectomy is warranted in eyes with severe endophthalmitis with a presenting vision of hand motions or less.<sup>[2,3]</sup> In an acute presentation; however, the view for the operating surgeon is often highly compromised. This occurs due to the concurrent presence of corneal edema, inflammatory membranes, or hemorrhage. Such situations often lead to incomplete or inadequate vitrectomy. These visual restrictions can be circumvented by the usage of an ophthalmic endoscope that allows visualization in the posterior segment by by-passing the hazy anterior segment.<sup>[4-7]</sup>

Many of these cases post-endophthalmitis resolution require a secondary corneal procedure for optical purposes and do undergo the same. In the current communication, we describe our series of endophthalmitis that underwent a primary endoscopic pars plana vitrectomy for infection management

and then at a later date underwent a definitive corneal optical procedure.

### Methods

This is a retrospective, non-comparative, consecutive case series conducted at a tertiary eye care center in south India. The study was approved by the institutional ethics committee (Ethics Ref. LEC 09-19-342). The data of all the patients were handled confidentially. As this was a retrospective study and only previous patient records were analyzed, the requirement of patient consent for the same was waived by the ethics committee. The study conformed to the tenets of the Declaration of Helsinki. Clinical and microbiologic records of all patients with endophthalmitis who underwent endoscopic vitrectomy between January 2015 and March 2019 and then subsequently underwent optical keratoplasty were reviewed and analyzed. Preoperatively, meticulous examination to rule out globe perforation and a B scan to rule out extensive choroidal

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<sup>1</sup>Smt. Kanuri Santhamma Center for Vitreoretinal Services, <sup>2</sup>Academy for Eye Care Education, <sup>3</sup>The Cornea Institute, Kallam Anji Reddy Campus, LV Prasad Eye Institute, Hyderabad, Telangana, <sup>4</sup>Retina-Vitreous Services, GMR Varalakshmi Campus, LV Prasad Eye Institute, Visakhapatnam, Andhra Pradesh, India

**Correspondence to:** Dr. Rajeev R Pappuru, Kallam Anji Reddy Campus, LV Prasad Eye Institute, Hyderabad - 500 034, Telangana, India. E-mail: rajeevkrp@gmail.com

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detachments were done to exclude such cases. All demographic and clinical information was collected from the patient's records.

All cases either underwent endoscopic pars plana vitrectomy endoscopy or underwent the endoscopic procedure after initial primary management based on the clinical decision. All patients underwent vitreous biopsy (tap), and empirical intravitreal vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL) were given. Based on culture reports, further interventions were planned. Vitreous samples were subjected to basic microbiological testing (calcofluor-white, Gram, and Giemsa stains) and culture (aerobic and anaerobic). All patients received topical antibiotics such as ciprofloxacin 0.3%, cycloplegics, and topical steroids, and oral ciprofloxacin 750 mg twice a day after the initial intervention.

### Success definition

The outcome at the last visit was evaluated in terms of anatomic and functional outcomes. A favorable anatomic outcome was defined as preservation of the globe, absence of hypotony, attached retina, and absence of active inflammation at the last visit. Functional success was defined as a vision of  $\geq 20/400$  at the last visit.<sup>[4,8-11]</sup> Evisceration was performed in cases that developed a painful blind eye, had a prolapse of intraocular contents due to a corneal perforation, or showed progression to panophthalmitis.

### Statistical analysis

The data were arranged on an Excel spreadsheet and analyzed using the statistical software MedCalcver 12.2.1.0 (Ostend, Belgium). Mean with standard deviation was reported for all normative data and the median was reported for nonnormative data. Proportional confidence intervals were computed and reported for all percentage comparisons. A *P* value  $<0.05$  was considered statistically significant.

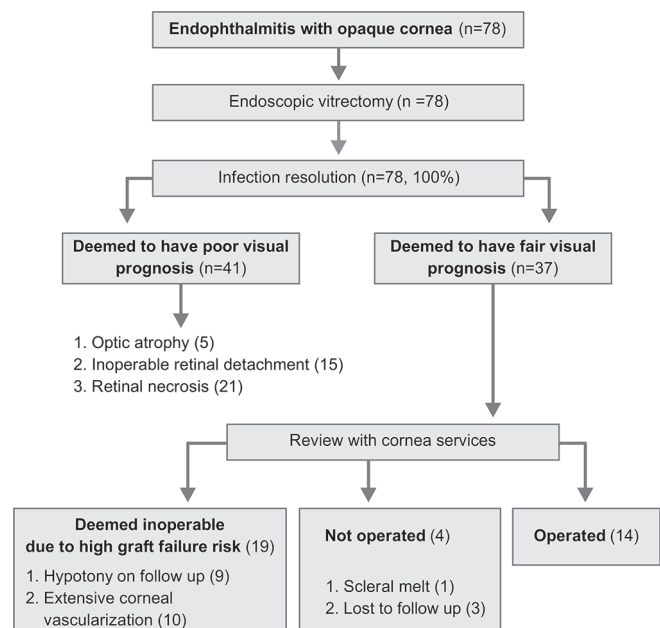
### Endoscopic technique

Endoscopy was done using the 20/23 G endoscope (E2 Laser and Endoscopy System; EndoOptiks, Inc, Little Silver, NJ, USA) with light and video dual function. The E2 Ophthalmic Laser Endoscopy System console houses endoscopic imaging and laser treatment capability. It includes a high-resolution video camera, 175 or 300 W xenon light source and an 810 nm diode laser. The endoscope probe presents a wide-field image and facilitates a panoramic intraocular view of the entire retina or a close-up (down to 0.75 mm) and a highly magnified view of any concurrent pathology. The in-built video adapter provides optimum zoom and manual focus of the endoscopic image. The resolution of the 20 G camera is 10,000 pixels while that of the 23 G camera is 6,000 pixels. The surgical steps included sterile draping of the eye and making two superior sclerotomies as per standard three-port vitrectomy surgery. The endoscope was then maneuvered to the mid-pupillary retrolental location and position was confirmed on the TV monitor. The vitrector was then positioned toward the endoscope in the vitreous cavity. Vitrectomy was then performed under endoscopic visualization. A thorough vitrectomy, to the extent possible, was attempted. The endpoint of surgery was taken as visibility of the disc and the retina. Wherever possible an attempt was made to induce posterior vitreous detachment (PVD). If a strong adherence was noted on the induction, PVD induction was avoided. All cases underwent a secondary optical keratoplasty at a later date.

## Results

In the defined time period, 78 eyes of 78 patients underwent endoscopic vitrectomy for endophthalmitis with the opaque cornea, of these 41 eyes were deemed unsuitable for further corneal management. The residual 37 eyes were deemed to have visual prognosis and were referred to cornea services for further management. Of those 37 eyes, nine eyes developed intractable hypotony, 10 developed extensive superficial and deep corneal vascularization, one developed sclera melt, and three patients were lost to follow-up. The current study thus included 14 eyes of 14 patients [Fig. 1].

There were 10 (90.9%) males and 1 (9.09%) female. The mean age at presentation was  $42.27 \pm 22.24$  years (median 36 years). There were 12 (85.7%) males and 2 (14.3%) females. The mean age at presentation was  $42.27 \pm 21.6$  years (median 36 years). Etiology-wise, eight cases (57.14%) were post-trauma, three cases (21.42%) post-keratoplasty, two cases (14.28%) were endogenous, and one case (7.14%) following corneal dermoid excision and wound melt. Culture positivity was in 5/14 (35.71%). The mean interval between endoscopic vitrectomy and keratoplasty was  $3.42 \pm 2.69$  months (median 2 months). The mean follow-up noted was  $20.42 \pm 11.45$  months (median 17.5 months). At the last visit, a favorable anatomic outcome was seen in 11/14 (78.57%) of cases and favorable functional outcome in 8/14 (57.14%) cases [Table 1, Figs. 2 and 3]. Microbiology evaluation revealed 5/14 (35.71%) to be culture positive. Among the corneal grafts, three grafts (21.42%) failed at the last recorded visit. Of the total eyes with an unfavorable visual outcome at the last visit, five patients had the potential for further visual improvement. This was concluded as one each had a potential for a regrant, astigmatism management, and a tarsorrhaphy release and two had a further planned silicone oil removal. One patient developed secondary glaucoma (Patient 11) and was implanted with an Ahmed glaucoma valve which achieved good control of intraocular pressure. Figure panels



**Figure 1:** Flowchart of all patients with endophthalmitis that underwent endoscopy

**Table 1: Demographic and clinical data of endophthalmitis cases undergoing endoscopic vitrectomy**

Case no.	Gender	Age	Presenting vision	Setting of endophthalmitis	Cause of poor visualization	Follow up in months	Final visual acuity	Final corneal graft status	Final anatomical outcome	Final visual outcome	Cause of low final vision	Further visual potential
1	M	36	HMCF	Trauma	Corneal infiltrate	30	20/400	Graft failure	F	F	Corneal edema	Y
2	M	21	HMCF	Post limbal dermoid excision	Corneal infiltrate	4	20/320	Clear	F	F	Silicone oil <i>in situ</i>	Y
3	M	86	HMCF	Post-keratoplasty	Corneal scar	15	HMCF	Corneal scar	F	UF	Corneal scar	Y
4	F	15	No PL	Endogenous	Corneal edema	18	PL	Clear	F	UF	Optic atrophy	N
5	M	57	HMCF	Post keratoplasty	Graft infiltrate	4	20/100	Clear with punctuate epithelial defects	F	F	Tarsorrhaphy <i>in situ</i>	Y
6	M	31	PL	Trauma	Corneal tear with infiltrate	4	Denies PL	Corneal scar	UF	UF	Hypotony and corneal scarring	N
7	M	76	PL	Corneal ulcer	Corneal ulcer	3	Denies PL	Corneal scar	UF	UF	Hypotony and corneal scarring	N
8	M	53	HMCF	Post-DSEK	Corneal infiltrate	2	20/200	Clear	F	F	Filamentary keratopathy and pale disc	N
9	M	16	PL	Open globe injury	Corneal edema and scarring	2	20/250	Clear	F	F	Astigmatism	Y
10	M	18	PL	Trauma with ciliary staphyloma	Ciliary staphyloma	2	PL	Corneal scarring	F	UF	Scarred cornea with vascularization	N
11	M	51	PL	Trauma	Corneal ulcer	11	20/60	Clear	F	F	Glaucomatous cupping	N
12	M	52	HM	Open globe injury	Corneal infiltrate	6	20/400	Clear	F	F	Oil-filled globe with corneal haze	Y
13	F	37	PL	Open globe injury	Corneal infiltrate	16	Denies PL	Clear	UF	UF	Recurrent closed funnel retinal detachment	N
14	M	34	PL	Open globe injury	Corneal infiltrate	17	20/200	Clear	F	F	Optic neuropathy	N

PL: Perception of light; HM: Hand motions vision; CFCF: Counting fingers close to face; PPV; Pars plana vitrectomy; EL: Endolaser, SOI: Silicone oil injection; IOFB: Intraocular foreign body; UF: Unfavorable; F: Favorable, Y: Yes, N: No



2 and 3 depict the pre- and postoperative clinical pictures for case numbers 13 and 14.

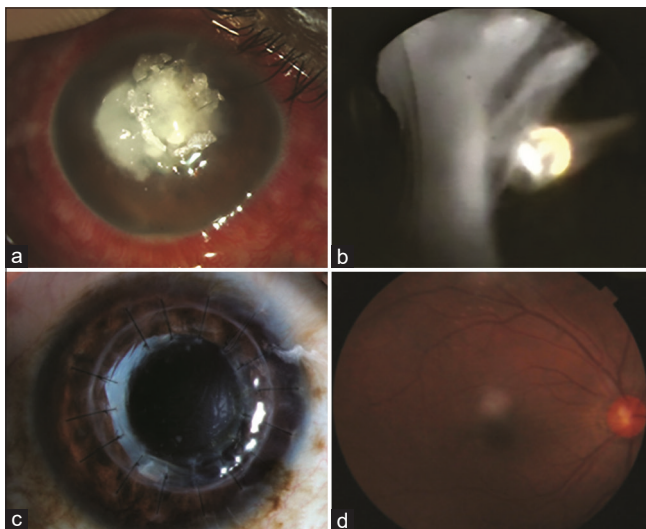
## Discussion

The current series reports the outcomes of endophthalmitis with opaque cornea managed with primary endoscopic vitrectomy and secondary keratoplasty. The endoscopic approach is a novel and effective approach to combat endophthalmitis with concurrent corneal pathology that precludes good visualization of the posterior segment and prevents thorough vitrectomy.<sup>[3,4,12]</sup> This approach allows adequate debulking of the vitreous cavity of the infected vitreous and also helps prognosticate the outcome at the first visit itself by potentially giving an opportunity of evaluating the retina and the optic disc. It is well known that the management of endophthalmitis becomes even more challenging and with poorer outcomes when it is associated with concurrent microbial keratitis or a pathology obscuring visualization of the posterior segment.<sup>[13]</sup> Thus, astute management of both modalities, the corneal pathology and the endophthalmitis, is warranted to realize the anatomic and functional benefits for the patients. This can be done either as a combined keratoplasty and pars plana vitrectomy at the same sitting or an initial endoscopic vitrectomy and then followed by a keratoplasty at a later date. Infection resolution in the current series was seen in 100% of cases

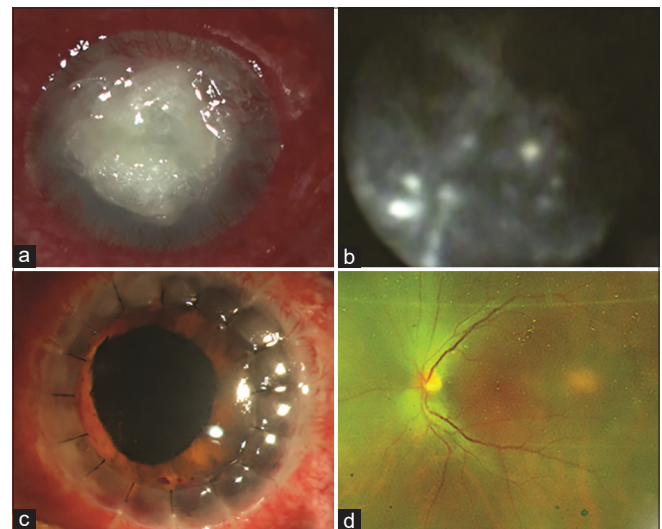
Dave *et al.* have published the largest series ( $n=43$ ) of combined keratoplasty and vitrectomy for endophthalmitis [Table 2].<sup>[14]</sup> In their series, 38 eyes had infectious keratitis, four eyes had bullous keratopathy, and one eye had a corneal scar. When compared to the current series, the number of cases with active corneal infection and the distribution of preoperative vision was comparable. The current series also had a comparable follow-up ( $P = 0.12$ ). While the postoperative visual outcomes were comparable for the lower visual acuities (perception of light and hand motions vision [HM]), for higher final visual acuities, there was a trend toward better outcomes by an initial primary endoscopic vitrectomy. The quantum of vision change from HM to at least counting

fingers close to face was higher in the current series with a primary endoscopic vitrectomy ( $P = 0.01$ ). The numbers of eyes that finally underwent phthisis or needed evisceration were statistically comparable but there was a clear trend toward lesser phthisis/evisceration in the current series [Fig. 4]. This could be due to better clearance of the vitreous cavity assisted by the enhanced endoscopic visualization. Residual infection at the last visit was seen in 10 (23.2%) eyes in that series while in the current series none showed residual infection at the last visit ( $P = 0.04$ ). Comparing the previous series of Dave *et al.* with our series, the percentage of eyes requiring repeat intravitreal antibiotics was 44.2% and 28.57% respectively. While the difference was statistically not significant, there was a trend toward the reduced necessity of repeat intravitreal injections in the endoscopy group. Comparing the previous series by Dave *et al.* with the current series, The percentage of eyes requiring a repeat vitrectomy procedure was 44.2% and 28.57% respectively. Again, while the difference was statistically not significant, there was a trend toward the reduced necessity of repeat vitrectomies in the endoscopy group. Corneal graft failure in their series was seen in 19/43 (44.2%) of eyes. In contrast, in our series, the graft failure rate was relatively lower and was noted in 3/14 (21.42%) eyes. This lower failure rate was possibly due to the fact that in the current series, the keratoplasty was deferred to a later date after the infection and inflammation in the eye were deemed to have settled. In contrast, in the series by Dave *et al.*, a simultaneous keratoplasty would have put the graft to the risk of failure due to surgery in a "hot" eye.

Dave *et al.* required the usage of temporary keratoprosthesis in 22 eyes (51.16%).<sup>[14]</sup> As is common knowledge, keratoprosthesis is a time consuming and challenging surgery. A temporary keratoprosthesis placement further obligates keratoprosthesis exchange and a penetrating keratoplasty after the pars plana vitrectomy is completed. This makes such procedures very cumbersome and requires a simultaneous multidisciplinary approach. As our current series used endoscopy to circumvent the corneal opacity, the surgery becomes relatively quicker without the need for multiple manipulations or long operating hours. Endoscopy also instantly picks up many cases that are



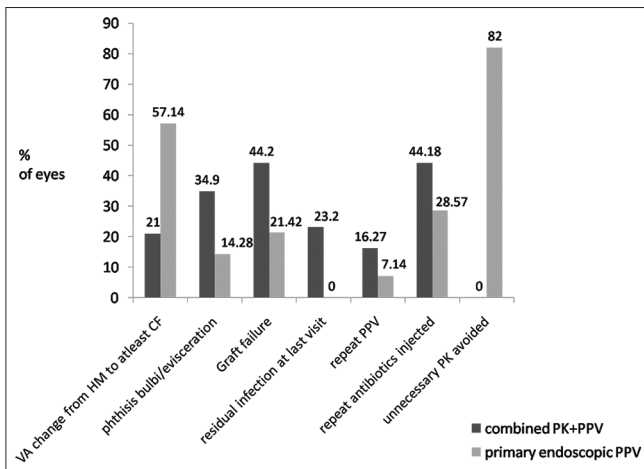
**Figure 2:** Case 13 showing (a) infectious keratitis with (b) endoscopic removal of the exudates, (c) postoperative slit-lamp photograph after keratoplasty, and (d) postoperative fundus photograph



**Figure 3:** Case 14 showing (a) infectious keratitis with (b) endoscopic removal of the exudates, (c) postoperative slit-lamp photograph after keratoplasty, and (d) postoperative fundus photograph

**Table 2: Comparison of the current series with the largest series performing combined penetrating keratoplasty and pars plana vitrectomy for endophthalmitis with opaque cornea**

	Largest series of combined keratoplasty and vitrectomy	Current series with primary endoscopic vitrectomy and secondary corneal graft	P for difference	95% C.I. for the difference
n	43	14		
Males (%)	26 (60.46%)	9 (85.7%)	0.08	
Active infectious corneal pathology (%)	38 (88.37%)	10 (71.42%)	0.13	
Pre-operative vision				
≤PL	35 (81.4%)	8 (57.14%)	0.06	6.22% to 56.66%
HM	5 (11.6%)	6 (42.85%)	0.01	
>HM	3 (6.9%)	0	0.37	
Mean follow up (months)	16.37±7.31	20.42±11.45	0.12	
Postoperative vision				
Denies PL	9 (20.93%)	3 (21.42%)	0.96	-0.29% to 42.68%
PL	13 (30.23%)	2 (18.18%)	0.4	2.96% to 55.53%
HM	1 (2.32%)	1 (9.09%)	0.29	
>HM to <20/400	12 (27.9%)	0	0.04	
≥20/400	11 (25.58%)	8 (57.14%)	0.03	
Change of vision from ≤HM to atleast CFCF	21%	57.14%	0.01	7.73% to 59.63%
Phthisis bulbi/evisceration	15 (34.9%)	2 (14.28%)	0.14	
Graft failures	19 (44.2%)	3 (21.42%)	0.13	
Number of eyes where unnecessary keratoplasties could be avoided	0	64/78 (82%)	<0.0001	69% to 89%
Residual infection at the last visit	10 (23.2%)	0	0.04	-0.58% to 37.68%
Eyes requiring repeat PPV	7 (16.27%)	1 (7.14%)	0.39	
Eyes requiring repeat intravitreal injections	19 (44.2%)	4 (28.57%)	0.3	



**Figure 4: Bar diagram showing a comparison of various elements between endoscopic vitrectomy and combined keratoplasty with vitrectomy**

otherwise inoperable further and do not have any prognosis as was seen in 41/78 eyes in this study. This avoids unnecessary corneal intervention in such cases and saves resources which are often limited in many setups. Assuming our entire subset of cases (78 eyes) was operated with a simultaneous keratoplasty, it would have amounted to an unnecessary extra intervention in 64/78 (82%) of the eyes. Nineteen eyes in our series were deemed inoperable by the cornea services due to the presence of high-risk factors for graft failure. Though such cases can be managed with options other than keratoplasty like keratoprosthesis, as per our

protocol, keratoprosthesis is not attempted in patients who have an otherwise seeing fellow eye.<sup>[15,16]</sup>

Tanaka *et al.* also reported their series of penetrating keratoplasty with vitrectomy for corneal opacity and posterior segment pathology.<sup>[17]</sup> Their series consisted of five cases with endophthalmitis. Of these five cases, three (60%) underwent phthisis as compared to 14.28% in our series ( $P = 0.05$ ). One eye (20%) in that series had a favorable functional outcome as compared to 11/14 (78.57%) in the current series ( $P = 0.02$ ). Lee *et al.* reported a series of 11 patients that underwent combined keratoplasty and pars plana vitrectomy using an Eckardt temporary keratoprosthesis.<sup>[18]</sup> In their series, six cases had a preoperative diagnosis of endophthalmitis. Three of those cases had concurrent keratitis while three had concurrent corneal opacity. Of these six cases, one case (16.66%) had a functionally successful outcome as compared to 11/14 cases (78.57%) in our series ( $P = 0.01$ ). Five out of the six eyes (83.83%) with endophthalmitis in that series developed corneal graft rejection as against three eyes (21.42%) in our series ( $P = 0.0008$ ).

The current study has some inherent weaknesses. Because of the retrospective nature of the study, the element of treating physician bias cannot be negated and may have a bearing on the final outcome. As trauma was a coexisting pathology in a few of the cases, the final outcome may also be partly due to the direct effect of the trauma rather than endophthalmitis alone. This again cannot be separated. The biggest limitation of the study is a very limited sample size as such cases require endoscopy which is still an emerging skill. This did not allow us to reach statistical significance for many outcome measures

which otherwise look clinically significant. The current study had cases, where the corneal ulcers/infiltrates did not clinically by themselves, merit a keratoplasty, rather merited medical management. Thus, removing the cornea in these cases to facilitate the posterior segment management would have led to an unnecessary keratoplasty without giving the eye an opportunity to heal nonsurgically. Even in cases where a keratoplasty is merited to control the infection, often the corneal clarity in the immediate postoperative period is not sufficient to allow an adequate vitrectomy.

Nevertheless, comparing our outcomes with previous studies where concurrent endophthalmitis and corneal pathology were managed by simultaneous keratoplasty and pars plana vitrectomy, we noted better functional outcomes a definite trend (though no statistical significance) toward better anatomic and functional outcomes, lesser incidence of phthisis or need for evisceration, lesser need for repeat vitrectomies or repeat intravitreal antibiotics, lesser graft failures and lesser residual infection post-procedure by attempting a primary endoscopic pars plana vitrectomy in such cases. In view of the paucity of such cases in the literature, a further multicentric pooled data analysis can shed further light on the advantage of primary endoscopy in such situations.

## Conclusion

Endoscopic vitrectomy allows for early intervention in endophthalmitis with the opaque cornea. This facilitates early resolution of infection, globe preservation, better graft survival, and fewer repeat posterior segment surgical intervention.

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## Conflicts of interest

There are no conflicts of interest.

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