

## A comparative analysis of surgical outcome in uveitic and non-uveitic steroid-induced glaucoma in children

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**Purpose:** To compare outcomes of surgical management of uveitic glaucoma (UG) and steroid-induced glaucoma (SIG) in children in terms of intraocular pressure (IOP) control, visual acuity, and associations for failure. **Methods:** This was a retrospective case-control study of consecutive UG (cases) and non-uveitic SIG (controls) in children <18 years of age who underwent surgery between January 2005 and December 2017. **Results:** Primary trabeculectomy with mitomycin C (MMC) was performed in 12 cases (mean age: 9.2 ± 4.3 years) and 40 controls (mean age: 10.4 ± 3.7 years) ( $P = 0.33$ ). Primary phaco-trabeculectomy with MMC was performed in 11 cases (mean age: 11.4 ± 4.7 years) and 16 controls (mean age: 10.4 ± 3.4 years) ( $P = 0.57$ ). IOP control ( $P = 0.26$ ), visual acuity ( $P = 0.97$ ), number of glaucoma medications ( $P = 0.06$ ), and survival rates (49% cases vs. 68% controls at 5 years;  $P = 0.22$ ) were similar between the two groups following trabeculectomy. Survival rates in the phaco-trabeculectomy group at 5 years were 68% cases vs. 69% controls ( $P = 0.71$ ). IOP was higher ( $P = 0.008$ ) and visual acuity was worse ( $P = 0.02$ ) in cases at the last visit. Associations for failure (univariate analysis) were younger age (OR: 6.29, 95% CL: 1.43, 27.67;  $P = 0.03$ ) and male gender (OR: 4.79, 95% CL: 1.09, 20.97;  $P = 0.04$ ). On multivariate analysis, younger age (OR: 11.985, 95% CL: 1.071, 134.153;  $P = 0.04$ ) remained significant. Preoperative number of uveitic attacks was protective on univariate (OR: 0.75, 95% CL: 0.48, 1.15;  $P = 0.1$ ) and multivariate analyses (OR: 0.49, 95% CL: 0.24, 0.09;  $P = 0.04$ ). **Conclusion:** Outcomes of trabeculectomy between cases and controls were similar in our series. However, phaco-trabeculectomy in pediatric uveitic eye group fared worse than eyes with SIG.

**Key words:** Pediatric uveitic glaucoma, phaco-trabeculectomy, secondary glaucoma, steroid-induced glaucoma, trabeculectomy

Uveitic glaucoma occurs in up to 35% of pediatric uveitis cases as reported in the literature.<sup>[1,2]</sup> This condition is included in the subgroup "glaucoma associated with acquired conditions" in the Congenital Glaucoma Research Network (CGRN) classification.<sup>[3]</sup> The reported prevalence of uveitic glaucoma in the pediatric population in southern India is quite low at 1.3%.<sup>[4]</sup> While the initial treatment consists of medical management with aqueous suppressants, surgery is resorted to when medical treatment fails to control elevated intraocular pressure (IOP). Various surgical modalities described in the management of pediatric uveitic glaucoma (UG) include goniotomy, trabeculectomy with adjunctive antimetabolites, trabeculodialysis, non-penetrating filtering surgery, and glaucoma drainage devices.<sup>[5-8]</sup> However, there is a paucity of information regarding the outcomes of glaucoma surgery in pediatric UG in the Indian subcontinent.

Surgical management of glaucoma with trabeculectomy in pediatric uveitic eyes is complicated by the fact that risk factors for failure are higher in this group despite the use of antimetabolites due to young age and a heightened

inflammatory response.<sup>[9]</sup> Visually significant cataract formation compounds this problem. The risk of cataract formation following trabeculectomy in young patients has been reported to be 24%.<sup>[10]</sup> Cataract formation in uveitic eyes and in those with steroid-induced glaucoma is similar to other types of glaucoma in this cohort. Since cataract and glaucoma<sup>[11-18]</sup> are features common to pediatric uveitis and steroid-induced glaucoma (SIG) in children, we proposed to compare the results of glaucoma filtering surgery between these two groups.

The aim of our study was to compare the outcomes of glaucoma filtering surgery in children who had undergone either trabeculectomy or phaco-trabeculectomy with adjunctive mitomycin C (MMC) between uveitic cases and cases diagnosed with non-uveitic steroid-induced glaucoma in the pediatric population. The primary outcome was IOP control at the last follow-up visit, and the secondary outcomes were visual acuity, complication rates, success rates, and associations for failure.

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## Methods

A retrospective case-control study of consecutive cases of uveitic glaucoma (23 eyes of 23 patients, i.e., cases) and non-uveitic steroid-induced glaucoma (56 eyes of 56 patients, i.e., controls; age- and gender-matched) who underwent primary filtering surgery between January 2005 and December 2017 at our institution was conducted. Children treated with steroids for the management of vernal keratoconjunctivitis were included as the control group. Institutional review board and ethics committee clearance were obtained prior to the study. Trabeculectomy with MMC was performed in 12 cases and in 40 controls. Phaco-trabeculectomy with MMC was performed in 11 cases and 16 controls who had visually significant cataracts. Patients <18 years of age at the time of surgery with a minimum follow-up period of 6 months were included.

Data abstracted from patient records included baseline demographics, etiology, classification of the type of uveitis according to the International Uveitis Study Group (IUSG)<sup>[19]</sup> classification system, details of preoperative assessment, intraoperative and postoperative complications, and details of examination at the last follow-up visit, including number of IOP-lowering and anti-inflammatory medications as well as the number of recurrent inflammatory episodes in the uveitic group. Data was censored after re-operation for uncontrolled IOP.

### Surgical technique

Surgery was performed under general anesthesia for all children.

The eye had to be quiescent for at least a period of 2 months prior to the surgery. Treatment with steroids and/or immunosuppressants was escalated 3 days prior to surgery in uveitic eyes.

### Trabeculectomy

The type of conjunctival flap (limbus/fornix based) was left to the surgeon's discretion. Two to three surgical sponges (Acumed devices, India) soaked in MMC (median concentration of 0.4mg/ml [IQR 0.2–0.4], for a median duration of one minute (IQR 1) (Biochem Pharmaceutical Industries Ltd., Daman, UT, India) were placed under the conjunctival surface. The surgical site was thoroughly irrigated with 30 ml of saline solution. A triangular scleral flap was fashioned 5/5/5 mm in dimension. The stoma was fashioned using a Kelly's punch, leaving an overlap of 1.5 mm on either side from the edges of the scleral flap. A peripheral iridectomy was performed. The scleral flap was sutured with a combination of either releasable or interrupted sutures using 10'0' monofilament nylon sutures. The conjunctiva was closed using 10'0' monofilament nylon sutures for fornix-based flaps and 8'0' polyglactin sutures for limbus-based flaps.

### Phaco-trabeculectomy

A single-site phaco-trabeculectomy with adjunctive MMC was performed. The trabeculectomy was performed as described above. The anterior chamber was entered using a 2.8 mm keratome from under the scleral flap. Phacoemulsification with implantation of a foldable hydrophobic intraocular lens (IOL) implant was then performed. Two cases and 3 controls underwent posterior curvilinear capsulorrhexis

with anterior vitrectomy following phacoemulsification. Trabeculectomy was then completed. The postoperative regimen of the uveitic cases consisted of application of topical steroids (1% prednisolone acetate); the dosage and tapering regimen were left to the surgeon's discretion. Systemic steroids and immunosuppressants were tapered depending on the inflammatory response. Topical prednisolone in a tapering schedule was used in all the controls. Patients were examined on the first postoperative day, the first two weeks, at the sixth week, and at regular intervals thereafter until the final follow-up visit or up to the last visit prior to re-operation.

### Definitions of success

Category A: Complete success: IOP >6 and <21 mmHg and >20% drop in IOP from the preoperative level, without medications.

Qualified success: IOP <21 mmHg with medications.

Failure: IOP <6 or >21 with medications, need for re-operation or laser treatment for elevated IOP, loss of light perception or the development of phthisis bulbi.

Category B: IOP >6 and <15 mmHg.

Postoperative titration procedures such as suture removal, needling, or argon laser suture-lysis were not considered as re-operations for IOP control.

### Statistical analysis

The Statistical Package for Social Sciences (SPSS version 20, SPSS Inc., Chicago IL, USA) was used for analysis. The eye was the unit of analysis. The independent samples Student *t* test was used for normally distributed data. Non-parametric tests such as the Mann-Whitney *U* test and Wilcoxon signed-rank test were used for data which were not normally distributed. Categorical data were analyzed with the Chi-squared and Fisher's exact test. Kaplan-Meier survival curves for the two groups were compared using the logrank test. Statistical significance was set at  $P < 0.05$ . The Cox proportional hazard model was used to assess associations for failure. Category A was used to define failure for this purpose. Multivariate analysis was carried out for associations with a significance of <0.2 on univariate analysis.

## Results

The baseline demographics of the trabeculectomy group are depicted in Table 1. The preoperative IOP was lower in cases (UG) compared to controls (SIG). Cases were more likely to present with synechial angle closure glaucoma compared to controls. Immunosuppressive medications were used in 4 cases; three were treated with methotrexate and one was treated with azathioprine. Similarly, in the phaco-trabeculectomy group, synechial angle closure was more frequent amongst cases [Table 1]. The number of anti-inflammatory medications was higher amongst cases. In all other respects, the two groups were similar. Four of the cases were on treatment with methotrexate at the time of surgery. The mean duration of steroid use among controls was  $23 \pm 12$  months in the trabeculectomy group and among cases was  $51.7 \pm 43$  months ( $P = 0.004$ ). The mean duration of steroid use among controls was  $25.7 \pm 16.2$  months in the phaco-trabeculectomy group and among cases was  $55.5 \pm 48.8$  ( $P = 0.001$ ).

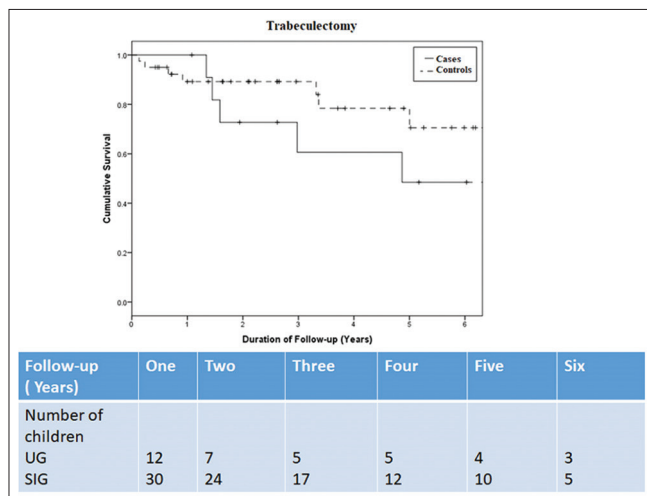
**Trabeculectomy**

Postoperative outcomes in terms of IOP control, number of IOP-lowering medications used, success rates, and visual acuity were similar in cases as well as in controls in the trabeculectomy group [Table 2]. Amongst cases, one patient developed a bleb leak which was managed conservatively and one developed hyphema which required an anterior chamber lavage. Postoperative titration was required in 3 cases: subconjunctival injections of 5-fluorouracil in one and argon laser suture lysis in the second, and needling of the bleb at 6 weeks in the third. One of the patients in the control group needed subconjunctival injections of 5-fluorouracil. Anti-inflammatory medications including steroids were required only amongst the cases at the final visit; none of the controls were on treatment with either topical or systemic steroids at their last visit. There were no significant differences in the success rates between the two groups, using either definition. Persistent hypotony at the last follow-up visit occurred in one patient in the trabeculectomy control group. The follow-up period was longer in the uveitic group with a mean of 4.1 years versus 3 years, but the difference was not statistically significant ( $P = 0.34$ ).

Kaplan–Meier survival analysis, using success category A, was 73%, 62%, and 49% for cases and 89%, 78%, and 68% for controls at the end of 1 year, 3 years and 5 years, respectively ( $P = 0.22$ ) [Fig. 1]. Re-operations were required in 6 cases and 4 controls [Table 2]. Cataract surgery was required in one case following trabeculectomy.

**Phaco-trabeculectomy**

Intraocular pressure was higher and use of IOP-lowering medications was greater at the final follow-up among cases [Table 2]. Improvement of visual acuity was better among controls. Postoperative inflammation requiring vitrectomy occurred in one eye amongst cases (UG). Five eyes in each group underwent Nd: YAG laser capsulotomy for posterior capsular opacification ( $P = 0.56$ ). Postoperative titration was required in 3 cases; one underwent argon laser suture lysis while two needed needling of the bleb. Only one patient in the control group required needling of the bleb. Re-operations for IOP control was required in two patients in the control group.



**Figure 1:** Kaplan–Meier survival analysis of cases and controls in the trabeculectomy group

There were no significant differences in the success rates, using either definition, between the two groups. Two eyes amongst cases in the phaco-trabeculectomy group developed loss of light perception at the last follow-up visit due to progression of glaucomatous optic nerve damage at the end of 18 and 36 months, respectively. The follow-up period was longer among cases with a mean of 4.4 years versus 2.5 years, but the difference was not significant ( $P = 0.19$ ).

Kaplan–Meier survival analysis using category A was 82%, 68%, and 68% for cases, and 93%, 93%, and 69% for controls at the end of 1 year, 3 years, and 5 years, respectively ( $P = 0.71$ ) [Fig. 2].

Comparison within groups [Supplemental Table 1].

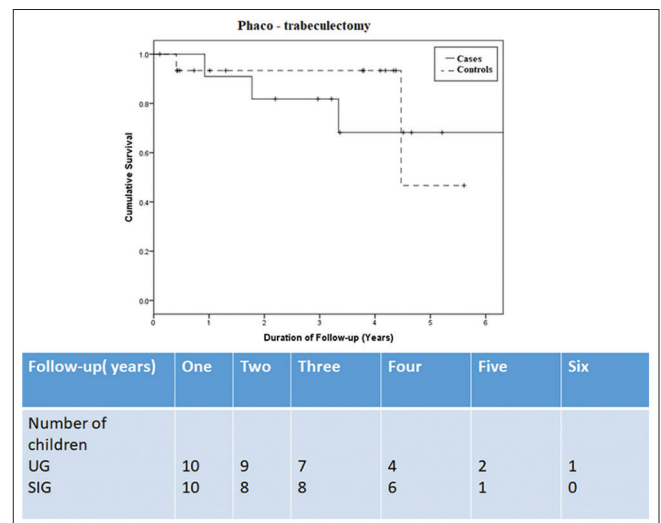
**Trabeculectomy**

There was a significant drop in IOP and number of IOP-lowering medications and improvement in visual acuity at the final follow-up visit among controls. While there was a significant drop in IOP and the number of IOP-lowering and anti-inflammatory medications among cases, there was no difference in the visual acuity at the final visit. A significant reduction in the number of recurrences of inflammation was seen among cases.

**Phaco-trabeculectomy**

There was a significant drop in IOP, number of IOP-lowering medications as well as improvement in visual acuity among controls in this group. Although there was a significant drop in the number of IOP-lowering medications, there was no change in either the IOP, number of anti-inflammatory medications or in the visual acuity among cases. However, there was a significant reduction in the number of recurrences of inflammation.

Associations analyzed for failure in the entire series are depicted in Supplemental Table 2. Younger age at the time of surgery and gender (males) were found to be significantly associated with failure on univariate analysis while the number of preoperative uveitic attacks were found to be protective. On multivariate analysis, younger age at the time of surgery



**Figure 2:** Kaplan–Meier survival analysis of cases and controls in the phaco-trabeculectomy group

**Table 1: Comparison of baseline demographics between Uveitic glaucoma (UG, Cases) and Steroid induced glaucoma (SIG, Controls)**

Trabeculectomy	Cases 12	Controls 40	Significance
Age at surgery (years)			
Mean±SD	9.2±4.3	10.4±3.7	0.33
IQR	7.2	5.7	
Gender			
M: F	10:2	25:15	0.17
Pre-operative BCVA (LogMAR)			
Mean±SD	0.77±0.74	0.97±0.87	0.65
IQR	1.32	1.6	
Pre-operative IOP (mmHg)			
Mean±SD	24±11.5	35.1±9.8	0.002
IQR	8.2	9.5	
Pre-operative number of IOP lowering medications			
Mean±SD	2.9±0.6	2.9±0.8	0.86
IQR	0.7	2	
Gonioscopy			
Open angles	9	40	0.001
Synechial angle closure	3	0	
Not available			
Diagnosis of uveitis			
IUSG classification			
Anterior uveitis	1		
Intermediate uveitis	4		
Posterior uveitis	6		
Pan uveitis	1		
Infectious	0		
Non-infectious	12		
Etiological diagnosis	6		
Unknown	0		
Juvenile Rheumatoid arthritis			
Sarcoidosis	3		
Vogt Koyanagi Harada syndrome	3		
Tuberculosis	0		
Pre-operative number of AIM			
Mean±SD	4.3±2.6	0.1±0.5	<0.05
IQR	5	0	
Type of AIM used			<0.05
Nil	0	36	
Topical steroids	2	3	
Systemic steroids	3	0	
NSAIDS	0	1	
Topical + Systemic steroids	3	0	
Topical + systemic steroids + Immunosuppressive	3	0	
Systemic steroids and Immunosuppressive	1	0	
Phaco-trabeculectomy	11	16	
Age at surgery (Years)			
Mean±SD	11.4±4.7	10.4±3.4	0.57
IQR	8	6.2	
Gender			
Male: Female	8:3	8:8	0.48
Pre-operative BCVA (Log MAR)			
Mean±SD	1.33±1.1	1.48±1.37	0.94
IQR	1.7	2.7	
Pre-operative number of IOP lowering medications			
Mean±SD	2.4±0.7	2.1±0.8	0.31
IQR	1	0	
Gonioscopy			
Open angles	6	16	0.003
Synechial closure	5	0	

Contd...



Table 1: Contd...

Trabeculectomy	Cases 12	Controls 40	Significance
Diagnosis of uveitis			
IUSG classification	1		
Anterior uveitis	4		
Intermediate uveitis	2		
Posterior uveitis	4		
Pan uveitis	2		
Infectious	9		
Non-infectious			
Etiological diagnosis	5		
Unknown	3		
Juvenile Rheumatoid arthritis	0		
Sarcoidosis	1		
Vogt Koyanagi Harada syndrome	2		
Tuberculosis			
Pre-operative number of AIM			
Mean±SD	3.9±S3.4	0.4±S0.1	0.004
IQR	7	0	
Type of AIM			
Nil	3	14	0.01
Topical steroids	1	0	
Systemic steroids	1	0	
NSAIDS	0	2	
Topical + Systemic steroids	2	0	
Topical + Systemic steroids + Immunosuppressives	2	0	
Systemic steroids + Immunosuppressives	2	0	

remained a significant association. The number of preoperative uveitic attacks remained protective.

## Discussion

Traditionally, trabeculectomy in childhood glaucoma has been associated with poor outcomes in terms of IOP control.<sup>[20]</sup> However, with the advent of anti-scarring agents, success rates have improved albeit at the risk of hypotony-related complications and increased rate of infections.<sup>[21,22]</sup> Glaucoma and cataract formation are common comorbidities in children with uveitis and vernal keratoconjunctivitis on long-term treatment with topical steroids.<sup>[13,17,18]</sup> Surgical treatment is resorted to when IOP remains uncontrolled on maximum tolerated medical treatment.

There is a paucity of information on the results of trabeculectomy and phaco-trabeculectomy for the management of uveitic and non-uveitic steroid-induced glaucoma in children. A summary of the results of trabeculectomy with modifications from the literature is mentioned in Table 3. Our results in terms of intraocular pressure control, complications, and success rates are like those published earlier. One of the disadvantages of using this technique in the pediatric population is that postoperative titration of filtration using releasable sutures, argon laser suture lysis, and use of 5-fluorouracil injections is often not possible in this age group due to the frequent necessity for repeated visits to the operation theater with their attendant risks. Argon laser suture lysis was possible in only one case and injections of 5-fluorouracil was possible in one uveitic case and one control in the trabeculectomy group in the outpatient setting in our series.

The outcomes of surgery in terms of IOP control, success rates, and re-operation rates were similar in both cases and

controls in our series. Although survival rates were better in the control group, the difference was not statistically significant. One would expect intraocular inflammation to be detrimental to success rates. However, the fact that we ascertained that inflammation was under control at the time of surgery and postoperative inflammation was appropriately managed may have favorably influenced our results. The number of anti-inflammatory drugs had reduced significantly by the last follow-up visit and so did the number of recurrences. Perioperative uveitis control has been shown to improve success rates of filtering surgery in uveitic eyes.<sup>[23]</sup> Changes in inflammatory activity were reported by Weise *et al.*<sup>[24]</sup> in 21 eyes in children with juvenile idiopathic arthritis (JIA) who underwent trabeculectomy with MMC. There was a significant drop in IOP from  $31.1 \pm 6.7$  to  $12.8 \pm 6.1$  mmHg in this group. Leinonen *et al.*<sup>[25]</sup> discuss the effects of tumor necrosis factor (TNF) inhibitors on trabeculectomy with MMC for patients with JIA-related uveitic glaucoma. IOP control following trabeculectomy with MMC lasted longer in those treated with TNF inhibitors (median of 3.2 years vs. 1.2 years in untreated eyes). The duration of steroid use was higher among cases in both surgical groups compared to controls. Perioperative escalation of anti-inflammatory therapy as well as the longer duration of steroid use among cases may have resulted in the reduced number of recurrences in our series.

Ang *et al.*<sup>[17]</sup> discussed the results of trabeculectomy with MMC in 8 eyes of six patients with severe vernal keratoconjunctivitis. Seven of the 8 eyes had successful IOP control for the duration of the follow-up; our results in the control group were similar. Senthil *et al.*<sup>[18]</sup> reported their results of surgical treatment of SIG in children. The IOP decreased significantly from  $30.3 \pm 13.3$  mmHg to  $13.1 \pm 13.9$  mmHg ( $P < 0.001$ ) in the trabeculectomy group.

**Table 2: Comparison of outcomes between Uveitic glaucoma (UG, Cases) and steroid induced glaucoma (SIG, Controls)**

Trabeculectomy	Cases	Controls	Significance
IOP at 6 weeks (mmHg)			
Mean±SD	17.2±13.9	11.5±5.6	0.59
IQR	27.5	9.7	
IOP at last visit (mmHg)			
Mean±SD	18.4±9.8	14.3±5.8	0.26
IQR	17.2	4.75	
BCVA (LogMAR) at 6 weeks			
Mean±SD	0.52±0.38	0.73±0.78	0.97
IQR	0.6	0.77	
BVCA (LogMAR) at last follow-up visit			
Mean±SD	0.5±0.5	0.53±0.75	0.34
IQR	0.6	0.47	
Number of IOP lowering medications at last visit			
Mean±SD	1.5±1.6	0.6±1.2	0.06
IQR	3	0.75	
Number of AIM at last visit			
Mean±SD	4.4±3.5		
IQR	7.75		
Follow-up period (Years)	4.1±3.9	3±2.3	0.34
Re-operations performed			
Re-trabeculectomy	2	4	0.43
Ahmed glaucoma valve implantation	1	2	
Diode Cyclophotocoagulation	1		
Outcomes:			
Category A			
Complete Success	5	28	0.16
Qualified Success	2	5	
Failures	5		
Category B		7	0.17
Complete Success	3	20	
Qualified Success	0	2	
Failures	9	18	
Phaco-trabeculectomy	11	16	
IOP (mmHg) at 6 weeks			
Mean±SD	19.1±8.3	12.6±5.2	0.01
IQR	8	4.75	
BCVA (LogMAR) at 6 weeks			
Mean±SD	0.71±1.02	0.5±0.67	0.71
IQR	0.6	0.57	
IOP (mmHg) at last follow-up visit			
Mean±SD	20.4±9.7	13.3±5.8	0.008
IQR	17	4.5	
BCVA (LogMAR) at last follow-up visit			
Mean±SD	1.39±1.23	0.45±0.7	0.02
IQR	2.52	0.7	
Number of AIM at last follow-up visit			
Mean±SD	2.4±3.7		
IQR	7		
Number of eyes requiring YAG Capsulotomy	5	5	0.56
Follow-up period (Years)	4.4±4.2	2.5±1	0.19
Re-operations performed			0.11
Ahmed glaucoma valve implantation	1	0	
Diode Cyclophotocoagulation	1	0	
Outcomes:			
Category A			
Complete Success	4	12	0.13
Qualified Success	4	2	
Failures	3	2	
Category B			
Complete Success	3	9	
Qualified Success	1	2	0.24
Failures	7	5	

**Table 3: Summary of literature results for surgical outcomes**

	Type of study (Sample size)	Type of uveitis	Type of surgery	Success criteria [Success (%)]
<b>Uveitic glaucoma</b>				
Heinz <sup>[7]</sup> (2011)	Retrospective (16)	Juvenile rheumatoid arthritis (JIA) - 12 Idiopathic-4	Trabeculectomy with MMC (0.2mg/ml)	IOP <21 mmHg±Medications (88)
Leionen <sup>[25]</sup> (2015)	Retrospective without Tissue Necrosis Factor inhibitors (14)	JIA-14	Trabeculectomy with MMC (0.4mg/ml)	IOP <21 mmHg (16) at 5 years
Leionen <sup>[25]</sup> (2015)	Retrospective with Tissue Necrosis Factor inhibitors (15)	JIA-15	Trabeculectomy with MMC (0.4mg/ml)	IOP <21 mmHg (73) at 5 years
Weise C <sup>[24]</sup> (2016)	Retrospective (21)	JIA-21	Trabeculectomy with MMC (0.2mg/ml)	Not available
Our study	Retrospective (12)	Idiopathic-6 Sarcoidosis-3 VKH-3	Trabeculectomy with MMC (0.4mg/ml)	IOP >6 and <21 mmHg (73) at one year (49) at 5 years
<b>Steroid induced glaucoma</b>				
Ang <sup>[17]</sup> (2012)	Retrospective (8)		Trabeculectomy with MMC (0.2mg/ml)	IOP <21 mmHg (87.5)
Senthil <sup>[18]</sup> (2020)	Retrospective (53)		Trabeculectomy Trabeculectomy with MMC Combined glaucoma surgery with lens aspiration and intraocular lens implantation	NA NA NA
Our study	Retrospective (40)		Trabeculectomy with MMC	IOP >6 and <21 mmHg (89) at one year (68) at 5 years

To the best of our knowledge, there are no reports on the results of combined cataract surgery with trabeculectomy in children with uveitis and limited information on the results of combined surgery in SIG in the pediatric age group. The outcomes in terms of IOP control and visual acuity were worse in the uveitic group compared to the SIG group in our series. However, there was a decrease in the number of recurrent episodes of inflammation in the phaco-trabeculectomy groups.

Younger age at the time of surgery has been found to be a risk factor for failure of filtration surgery.<sup>[22]</sup> Associations with failure in our series included younger age at the time of surgery and male gender on univariate analysis. A diagnosis of uveitic glaucoma was not found to be a significant association. On multivariate analysis, only younger age remained a significant risk factor. The number of pre-operative uveitic attacks were found to be protective in terms of IOP control both on univariate and multivariate analyses in our series. This could be attributed to the deleterious effect of inflammatory mediators on the function of the ciliary body.<sup>[26]</sup> This suggests that the need for further surgical intervention in uveitic eyes may not be required as often as in eyes with normal ciliary body function.

Our study has several limitations. The sample size in the uveitic group was small. However, most of the published series on surgical management of glaucoma in pediatric uveitis show small sample sizes as well [Table 3]. The mechanism of glaucoma in uveitic eyes is multifactorial, and steroids do contribute to IOP elevation in these eyes.<sup>[27]</sup> Although we excluded uveitic eyes with a clear temporal association with the use of steroids and IOP elevation, we could not completely isolate this mechanism from the cases included in our study.

## Conclusion

There were no significant differences in the outcomes of trabeculectomy surgery between cases and controls in our series. However, phaco-trabeculectomy in uveitic eyes in the pediatric age group did not perform as well as the eyes with SIG. Postoperative recurrences of inflammation reduced in the UG in both surgical techniques. The number of preoperative episodes of inflammation was found to be protective in terms of IOP control.

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## Conflicts of interest

There are no conflicts of interest.

## References

- Heiligenhaus A, Niewerth M, Ganser G, Heinz C, Minden K; German Uveitis In Childhood Study Group. Prevalence and complications of uveitis in juvenile rheumatoid arthritis in a population-based nation-wide study in Germany: Suggested modification of the current screening guidelines. *Rheumatology (Oxford)* 2007;46:1015-9.
- Sijssens KM, Rothova A, Berendschot TT, De Boer JH. Ocular hypertension and secondary glaucoma in children with uveitis. *Ophthalmology* 2006;113:859.
- Thau A, Lloyd M, Freedman S, Beck A, Grajewski A, Levin AV. New classification for paediatric glaucoma; Implications for clinical care and a research registry. *Curr Opin Ophthalmol* 2018;29:385-94.

4. Narayana KM, Bora A, Biswas J. Patterns of uveitis in children presenting at a tertiary eye care center in south India. *Indian J Ophthalmol* 2003;51:129-32.
5. Bohnask BL, Freedman SF. Surgical outcomes in childhood uveitic glaucoma. *Am J Ophthalmol* 2013;155:134-42.
6. Kanski JJ, McAllister JA. Trabeculodialysis for inflammatory glaucoma in children and young adults. *Ophthalmology* 1985;92:927-30.
7. Heinz C, Koch JM, Heiligenhaus A. Trabeculectomy or modified deep sclerectomy in juvenile uveitic glaucoma. *J Ophthalmic Inflamm Infect* 2011;1:165-70.
8. Kafkala C, Hynes A, Choi J, Topalkara A, Foster CS. Ahmed valve implantation for uncontrolled pediatric uveitic glaucoma. *J AAPOS* 2005;9:336-40.
9. Papadapoulou M, Edmunds B, Fenerty C, Khaw PT. Childhood glaucoma surgery in the 21<sup>st</sup> century. *Eye* 2014;28:931043.
10. Adelman RA, Brauner SC, Afshari NA, Grosskreutz CL. Cataract formation after initial trabeculectomy in young patients. *Ophthalmology* 2003;110:625-9.
11. Gupta S, Shah P, Grewal S, Chaurasia AK, Gupta V. Steroid-induced glaucoma and childhood blindness. *Br J Ophthalmol* 2015;99:1454-56.
12. Smith JA, Mackensen F, Sen NH, Leigh JF, Watkins AS, Pyatetsky D, *et al.* Epidemiology and course of disease in childhood uveitis. *Ophthalmology* 2009;116:1544-51.
13. Esen E, Sismaz S, Balci S, Ekinci RMK, Demircan N. Clinical features of childhood uveitis at a tertiary referral center in Southern Turkey. *Int Ophthalmol* 2021;41:2073-81.
14. Gautam N, Singh R, Agarwal A, Yangzes S, Dogra M, Sharma A, *et al.* Pattern of pediatric uveitis at a tertiary referral center in North India. *Ocul Immunol Inflamm* 2018;26:379-85.
15. Takkar B, Venkatesh P, Gaur N, Garg SP, Vohra R, Ghose S. Pattern of uveitis in children at the apex institute for eye care in India: Analysis and review of literature. *Int Ophthalmol* 2018;38:2061-8.
16. Ganesh SK, Bala A, Biswas J, Ahmed AS, Kempen JH. Pattern of pediatric uveitis seen at a tertiary referral center from India. *Ocul Immunol Inflamm* 2016;24:402-9.
17. Ang M, Ho CI, Tan D, Chan C. Severe vernal keratoconjunctivitis requiring trabeculectomy with Mitomycin C for corticosteroid-induced glaucoma. *Clin Exp Ophthalmol* 2012;40:e149-55.
18. Senthil S, Thakur M, Rao HL, Mohamed A, Jonnadula GB, Sangwan V, *et al.* Steroid-induced glaucoma, and blindness in vernal keratoconjunctivitis. *Br J Ophthalmol* 2020;104:265-9.
19. Deschenes J, Murray PI, Rao NA, Nussenblatt RB. International Uveitis Study Group (IUSG): Clinical classification of uveitis. *Ocul Immunol Inflamm* 2008;16:1-2.
20. Beauchamp GR, Parks MM. Filtering surgery in children: Barriers to success. *Ophthalmology* 1979;86:170-80.
21. Mandal AK, Walton DS, John T, Jayagandan A. Mitomycin C-augmented trabeculectomy in refractory congenital glaucoma. *Ophthalmology* 1997;104:996-1001.
22. Al-Hazmi A, Zwaan J, Awad A, Mullaney PB, Wheeler DT. Effectiveness and complications of MMC use during pediatric glaucoma surgery. *Ophthalmology* 1998;105:1915-20.
23. Magliyah MS, Badawi AH, Alshamrani AA, Malik R, Al-Dhibi H. The effect of perioperative uveitis control on the success of glaucoma surgery in uveitic glaucoma. *Clin Ophthalmol* 2021;15:1465-75.
24. Weise C, Heiligenhaus A, Heinz C. Changes in inflammatory activity after glaucoma filtration surgery in children with chronic anterior uveitis. *Ocul Immunol Inflamm* 2016;24:397-401.
25. Leinonen S, Kotaniemi K, Kivela T, Majander A. Potential effect of tumor necrosis factor inhibitors on trabeculectomy with Mitomycin C for patients with juvenile idiopathic arthritis-related uveitic glaucoma. A retrospective analysis. *JAMA Ophthalmol* 2015;133:1323-8.
26. Majumder PM, Burugupalli K, Menia NK, Ganesh SK, Biswas J. Pattern of uveitic hyptony in a tertiary eye hospital in India. *Ocul Immunol Inflamm* 2018;26:924-8.
27. Kothari S, Foster CS, Pistilli M, Liesegang T, Daniel E, Sen HN, *et al.* The risk of intraocular pressure elevation in pediatric non-infectious uveitis. *Ophthalmology* 2015;122:1987-2001.



**Supplemental Table 1: Comparison of outcomes within each group**

	Pre-operative	At last follow-up	Significance
Trabeculectomy group- Cases			
IOP (mmHg) Mean±SD	38.5±5.7	18.4±9.8	0.003
BCVA (LogMAR) Mean±SD	0.77±0.724	0.49±0.49	0.24
Number of IOP lowering medications Mean±SD	2.9±0.6	1.5±1.6	0.02
Number of AIM Mean±SD	2.06±0.85	0.25±0.57	0.001
Number of uveitic attacks	3.5±1	0.6±1.9	0.05
Trabeculectomy Controls			
IOP (mmHg) Mean±SD	31±7.2	14.3±5.9	0.05
BCVA (LogMAR) Mean±SD	0.96±0.87	0.52±0.75	0.05<0.05
Number of IOP lowering medications Mean±SD	2.9±0.9	0.6±1.2	
Number of AIM Mean±SD	0.1±0.5	0	
Phaco-trabeculectomy Cases			
IOP (mmHg) Mean±SD	26.3±12.2	20.4±9.7	0.28
BCVA (LogMAR) Mean±SD	1.32±1.1	1.39±1.2	0.99
Number of IOP lowering medications Mean±SD	2.4±0.7	0.8±1	0.007
Number of AIM Mean±SD	3.9±3.4	2.4±3.7	0.37
Number of uveitic attacks	3.2±3.3	0.9±1.8	<0.05
Phaco-trabeculectomy Controls			
IOP (mmHg) Mean±SD	24.3±9.2	13±5.8	0.002
BCVA (LogMAR) Mean±SD	1.5±1.4	0.4±0.7	0.002
Number of IOP lowering medications Mean±SD	2.1±0.8	0.2±0.6	0.001
Number of AIM Mean±SD	0.4±1	0	

**Supplemental Table 2: Associations for failure in the surgical groups using Cox proportional hazard model**

	Odds ratio	95% Confidence limits	Significance
Univariate analysis			
Gender (Male)	4.792	1.095,20.971	0.037
Age <10 years a time of surgery	6.293	1.434,27.617	0.01
Pre-operative IOP (mmHg)	1.004	0.949,1.062	0.894
Pre-operative BCVA	1.121	0.71,1.769	0.624
Pre-operative number of AIM	1.1	0.92,1.312	0.29
Pre-operative number of uveitic attacks	0.75	0.485,1.159	0.195
Paediatric uveitis	1.73	0.666,4.494	0.261
Trabeculectomy	1.158	0.404,3.32	0.784
Multivariate analysis			
Gender (Male)	0.349	0.041,2.954	0.334
Age <10 years at surgery	11.985	1.071,134.153	0.04
Pre-operative attacks of uveitis	0.493	0.24,0.995	0.04