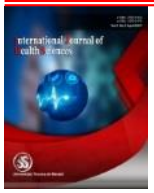

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Factors Associated with Outcomes of Intravitreal Triamcinolone Injection Among Pseudophakic Cystoid Macular Edema Patients at KCMC from 2017 to 2023

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pseudophakic cystoid macular edema;
topical corticosteroids;

Abstract

Background: Pseudophakic cystoid macular oedema (PCME), also known as Irvine–Gass syndrome, is a postoperative complication of cataract surgery characterized by cystic retinal changes and potential vision loss. Intravitreal triamcinolone acetonide (IVTA) is used as a treatment due to its potent anti-inflammatory effects, although standardized protocols are lacking. Aim: To evaluate the outcomes and factors associated with IVTA injections among PCME patients treated at Kilimanjaro Christian Medical Centre (KCMC) between January 2017 and December 2023. Methodology: A retrospective cohort study was conducted involving PCME patients treated with a single 4 mg IVTA injection. Data on visual acuity (VA) and central macular thickness (CMT) were collected at baseline, and at one, three-, and six-months post-treatment. VA was assessed using the Snellen chart and converted to logMAR for analysis. Descriptive and inferential statistical methods were used to evaluate treatment outcomes and identify associated factors. Results: A total of 90 eyes from 86 patients were included. Mean VA improved from 1.13 logMAR at baseline to 0.80 logMAR at six months. Mean CMT decreased from 498.0 µm to 339.7 µm over the same period. Better baseline VA was significantly associated with visual improvement, while younger age and single injection were predictors of favorable anatomical outcomes. Conclusion: IVTA is effective in improving visual acuity and reducing macular thickness in PCME patients. Better baseline vision, younger age, and single-dose treatment were associated with greater treatment success, supporting IVTA use in clinical management, especially in resource-limited settings.

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Contents

1 Introduction

Cataract remains the leading cause of blindness globally, and while cataract surgery is generally safe and widely performed (1; 2)Pseudophakic Cystoid Macular Edema (PCME), or Irvine-Gass syndrome, remains a common postoperative complication that can impair visual recovery (Yonekawa & Kim, 2012a; McCafferty et al., 2017; Lobo, 2012). PCME typically occurs 4 to 6 weeks after surgery and is more common among individuals with risk factors such as diabetes, hypertension, complicated surgeries, or pre-existing retinal conditions (Guo et al., 2015).

Pathogenesis of PCME following cataract surgery is uncertain, but postoperative inflammation is considered the primary cause, leading to disruption of the blood-retinal barrier and accumulation of fluid in the macula (Guo et al., 2015). Clinical symptoms include visual decline, metamorphopsia, and central scotomas, and diagnosis is supported by OCT and other imaging modalities (Han et al., 2019; Thesis & Drukkerijen, 2024).

Management of PCME includes NSAIDs and corticosteroids; however, there is no standard treatment to date (Guo et al., 2015; Ahmadyar et al., 2023; Thesis & Drukkerijen, 2024). Intravitreal triamcinolone acetonide (IVTA), a potent corticosteroid with anti-inflammatory and anti-VEGF properties, has shown promise in improving visual and anatomical outcomes by delivering the drug directly to the affected site. (Guo et al., 2015; Tariq et al., 2022)

Several studies have investigated the temporal dynamics of outcomes following IVTA administration, shedding light on the efficacy and variability of treatment response over time (Kuley et al., 2021; Kasthuribai et al., 2023). At KCMC, IVTA has been used to treat pseudophakic cystoid macular edema patients, though its effect and factors associated with treatment outcome are unknown.

To the best of my knowledge there is limited published work on factors associated with treatment outcomes after intravitreal triamcinolone injection(IVTA) among pseudophakic cystoid macular edema patients in sub-Saharan Africa and East Africa including Tanzania, this study aims to assess the outcomes of IVTA for PCME at KCMC and its identifiable factors associated with its effectiveness, by focusing on assessing visual acuity and macular thickness by using OCT following treatment with intravitreal triamcinolone acetonide in order improve the management and prognosis of PCME in our setting, potentially leading to better visual outcomes and enhanced quality of life for affected individuals (Iftikhar et al., 2023).

2 Materials and Methods

This retrospective cohort study was conducted at the Ophthalmology Department of Kilimanjaro Christian Medical Centre (KCMC) in northern Tanzania, covering the period from January 2017 to December 2023. The study included patients diagnosed with pseudophakic cystoid macular edema (PCME) who were treated with intravitreal triamcinolone acetonide (IVTA). Patients with other ocular comorbidities, a history of combined

ocular surgery, cataract surgery performed more than one year prior, or those who received other forms of corticosteroids within three months before or during the follow-up period were excluded.

Ethical approval was granted by the KCMU College Research and Ethical Review Committee (No. PG142/2024), and permission to access patient records was obtained from the Head of the Ophthalmology Department. Patient data were identified from the minor theatre registry and retrieved from both hard copy files and the electronic health management system (EHMS). Relevant variables, including demographics, clinical characteristics, and treatment outcomes such as visual acuity and central macular thickness (CMT), were extracted at baseline, one, three, and six months post-injection. Visual acuity was measured using the Snellen chart and converted to logMAR units for analysis.

Data were analyzed using STATA version 17. Descriptive statistics were used to summarize variables, while paired t-tests and chi-square tests assessed differences in outcomes over time and between groups. A generalized linear model (GLM) with Poisson distribution and log link was applied to determine the association between clinical factors and treatment outcomes, presented as relative risks (RR) with 95% confidence intervals. Both univariate and multivariable analyses were conducted, with statistical significance set at $p < 0.05$.

3 Results and Discussions

3.1 Results

A total of 789 patients were identified from the minor theater registry book, and 664 patients' files were retrieved from the medical records facility. Among these, 142 patients' files had pseudophakic cystoid macular edema; however, only 86 patients (90 eyes) had files that met the inclusion criteria and were enrolled in the study.

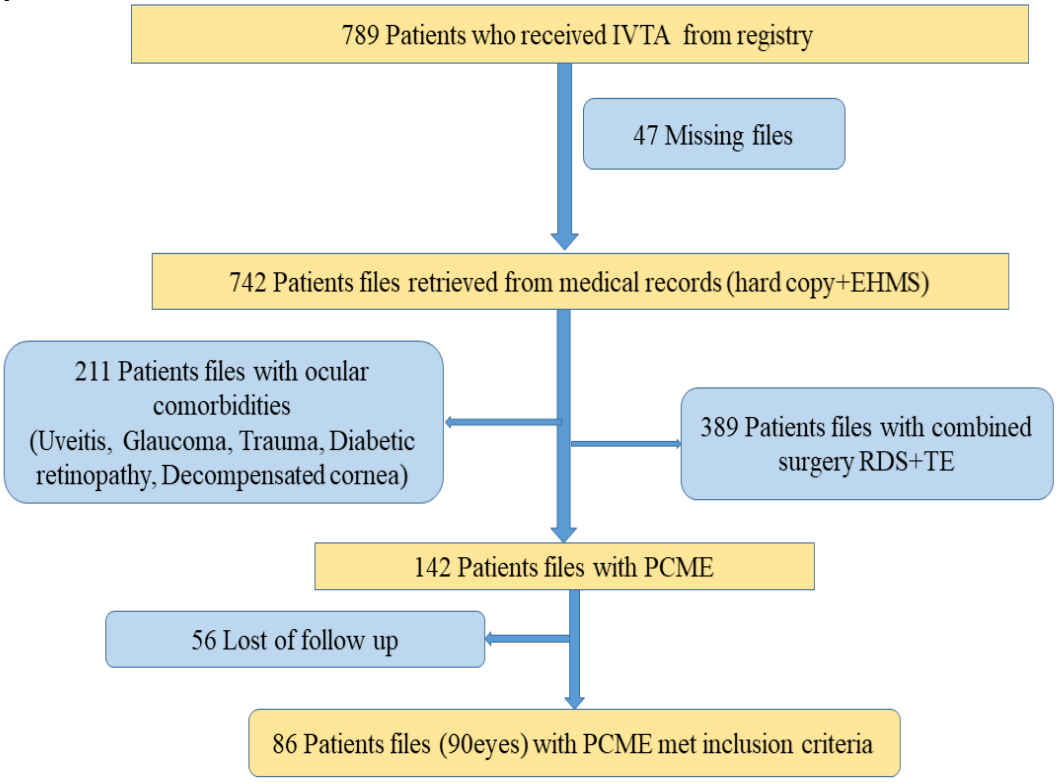

Figure 1: Flow chart for recruitment of study participants

This study included 90 eyes from 86 patients treated with 4 mg intravitreal triamcinolone acetonide (IVTA) for pseudophakic cystoid macular edema (PCME) at the KCMC eye clinic between January 2017 and December 2023. The majority of participants were male (63.3%), with females comprising 36.7%, and the median age was 73 years (IQR: 64–81), with 58.9% aged 70 or older. Laterality was nearly evenly distributed, with 51.1% treated in the right eye and 48.9% in the left. Regarding systemic comorbidities, 21.1% had diabetes mellitus, and 35.6% had hypertension. Most participants (77.8%) underwent extracapsular cataract extraction, while 22.2% had phacoemulsification. Acute PCME was present in 63.3% of cases, and chronic PCME in 36.7%, with 14.4% having a history of vitreous loss during cataract surgery. Overall, 57.8% received a single IVTA injection, whereas 42.2% required multiple injections. (**Table1)**

Table 1
Participants' background characteristics (N=90 eyes)

Characteristics	n	%
Sex of the patient		
Male	57	63.3
Female	33	36.7
Age of participant (in years)		
<70	37	41.1
≥70	53	58.9
Median (IQR)	*73 (64-81)*	
Laterality		
Right eye	46	51.1
Left eye	44	48.9
Diabetes status		
No	71	78.9
Yes	19	21.1
Hypertension status		
No	58	64.4
Yes	32	35.6
Duration post cataract in months		
≤6 months	57	63.3
>6 months	33	36.7
Type of surgery		
Phaco	20	22.2
Ecce	70	77.8
Number of injections		
1	52	57.8
>1	38	42.2
Vitreous loss		
No	77	85.6
Yes	13	14.4
VA at baseline		
≤11log MAR	46	51.1
>11log MAR	44	48.9
Final Macular Thickness		
≤250	37	41.1
>250	53	58.9
Final VA		
≤1log MAR	64	72.3
>1log MAR	26	27.7

Visual Outcome

Figure 1 shows the mean changes in visual acuity (VA), measured in log MAR units, from baseline to one, three, and six months of follow-up. Higher visual acuity is indicated by lower values on the log MAR scale. The visual acuity improved significantly from baseline to six months of follow-up. At baseline there was severe visual impairment with the mean visual acuity of 1.13(95%CI: 1.02-1.24 SD ±0.51) which increased to 0.90 (95%CI: 0.80–1.01; SD ±0.48) at one month, 0.78(95%CI: 0.67–0.88; SD ±0.50) at three months, and 0.80 (95%CI: 0.68–0.91; SD ±0.54) at six months of follow up. Despite the slight decrease in vision at six months, the improvement of visual acuity from baseline to one month, three months, and six months was statistically significant ($p < 0.001$).

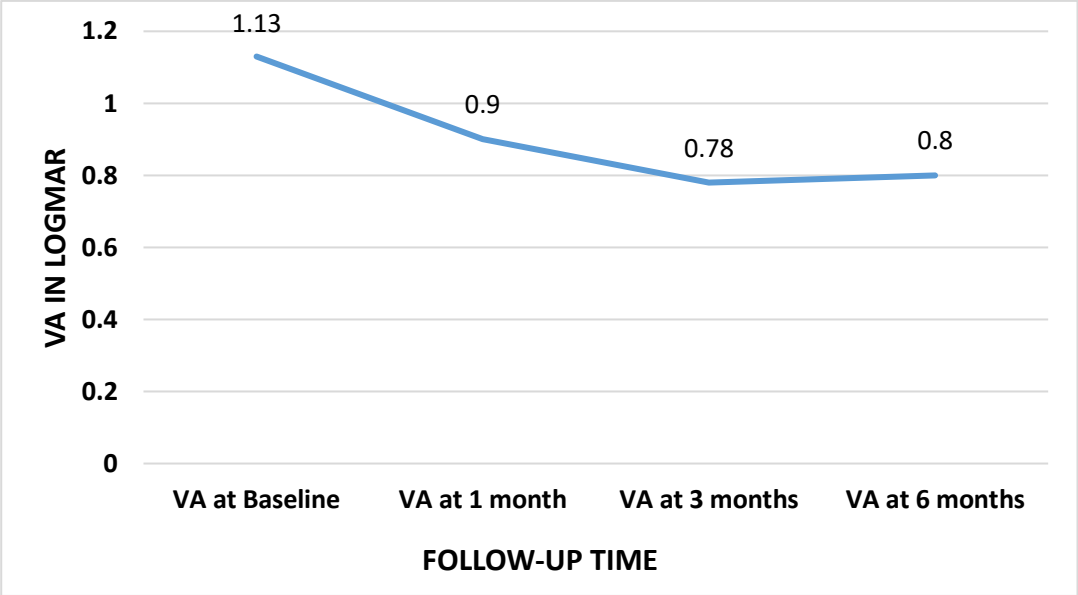

Figure 1. Mean visual acuity change in log MAR from baseline to six months of follow-up

Anatomical Outcome

With regard to central macular thickness (CMT), as measured by optical coherence tomography, a significant reduction was observed over a six-month follow-up period. The baseline mean CMT was 498.03 µm (95%CI: 467.95–528.12 µm), decreased to 353.63 µm (95%CI: 326.14–381.13µm; $p<0.001$) at one month, 325.99 µm (95%CI: 297.97–354.02; $p<0.001$µm) at three months, 339.74 µm (95%CI: 310.54–368.95µm; $p<0.001$) at six months. Despite the slight increase in CMT at six months, the CMT remained statistically significantly compared to baseline, indicating sustained improvement following IVTA injection ($p<0.001$)(Figure 3).

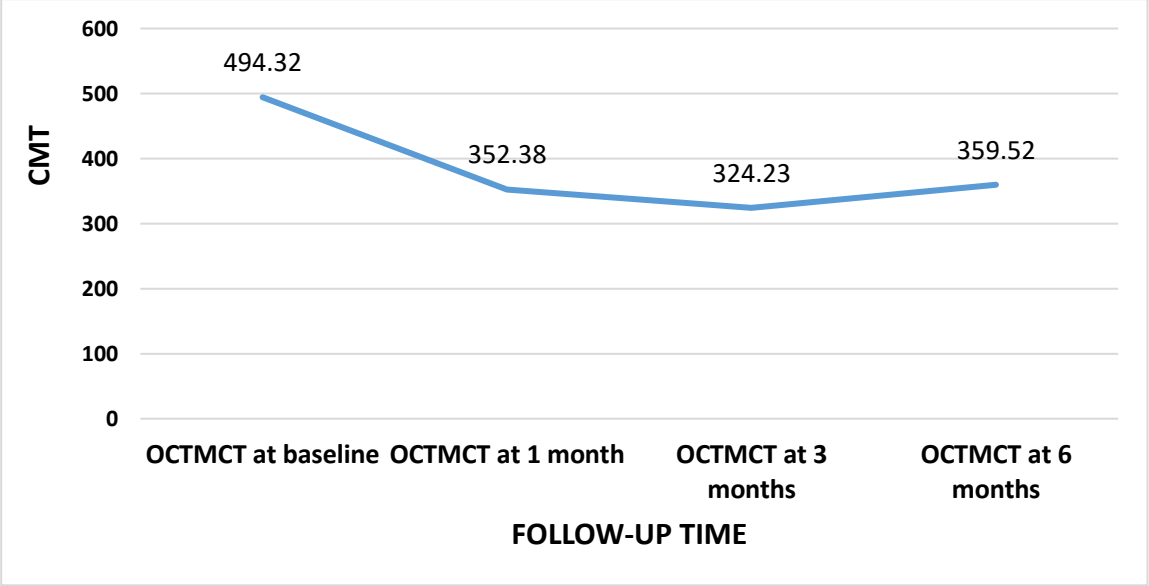

Figure 3. Mean CMT change from baseline to six months of follow-up

Factors Associated with Best Corrected Visual Acuity (BCVA)

In the crude analysis, only baseline VA showed a significant association with BCVA. Eyes with baseline VA >1logMAR were 45% less likely to achieve BCVA (CRR = 0.55; 95% CI: 0.41–0.72; p < 0.001). In adjusted analysis, baseline VA remained significantly associated with BCVA (ARR = 0.54; 95% CI: 0.40–0.71; p < 0.001) (**Table 4)**

Factors Associated with Central Macular Thickness (CMT)

In crude analysis, age, duration post cataract, and number of injections showed a significant association with CMT. Eyes of participants aged ≥70 years were 41% less likely to have success in CMT compared to eyes of participants aged <70 years (CRR=0.59; 95%CI: 0.35-0.98; P-value =0.041) across the patients. Eyes with >6 months duration post cataract were 52% significantly less likely to have success in CMT (CRR=0.48; 95%CI: 0.24-0.91; P-value =0.025) compared to eyes with ≤6 months duration post cataract across the patients. In terms of the number of injections, eyes that had >1 injection were 62% less likely to have success in CMT compared to eyes that had a single injection (CRR=0.38; 95%CI: (0.19-0.72; P-value =0.003) across the patients.

Adjusted for other factors, age and number of injections remained significantly associated with CMT. Eyes of participants aged ≥70 years were 38% less likely to have success in CMT compared to eyes of participants aged <70 years (ARR=0.62; 95%CI: 0.38-0.99; P-value =0.045) and eyes that had >1 injection were 59% less likely to have success in CMT compared to eyes that had 1 injection (ARR=0.41; 95%CI: (0.21-0.77; P-value =0.006) across the patient. (**Table 5**)

Table 4
Factors associated with BCVA

Characteristic	CRR (95%CI)	P-value	ARR (95%CI)	P-value
Age of the participants (In years)				
<70	Ref		Ref	
≥70	0.83(0.65-1.07)	0.159	0.91(0.73-1.14)	0.418
Sex of the patient				
Male	Ref		Ref	
Female	1.19(0.93-1.52)	0.152	0.99(0.80-1.25)	0.991
Diabetes status				
No	Ref		Ref	
Yes	0.92(0.65-1.28)	0.614	0.78(0.58-0.10)	0.084
Hypertension status				
No			Ref	
Yes	1.04(0.79-1.35)	0.795	1.16(0.92-1.46)	0.223
Duration post cataract in months				
≤6 months	Ref			
>6 months	1.05(0.82-1.35)	0.684		
Type of surgery				
Phaco	Ref			
ecce	0.82(0.65-1.05)	0.113		
Number of injections				
1	Ref			
>1	0.83(0.64-1.08)	0.175		
Vitreous loss				
No	Ref			
Yes	0.59(0.33-1.07)	0.085		
VA at baseline				
≤1logMAR	Ref		Ref	
>1logMAR	0.55(0.41-0.72)	<0.001	0.54(0.40-0.71)	<0.001

Table 5
Factors associated with CMT

Characteristic	CRR (95%CI)	P-value	ARR (95%CI)	P-value
Age of the participants (In years)				
<70	Ref		Ref	
≥70	0.59(0.35-0.98)	0.041	0.62(0.38-0.99)	0.045
Sex of the patient				
Male	Ref		Ref	
Female	0.73(0.41-1.28)	0.273	0.75(0.45-1.24)	0.259
Diabetes status				
No	Ref		Ref	
Yes	1.03(0.56-1.89)	0.922	0.72(0.39-1.30)	0.273
Hypertension status				
No	Ref		Ref	
Yes	1.10(0.65-1.86)	0.714	1.25(0.79-1.99)	0.328
Duration post cataract in months				
≤6 months	Ref		Ref	
>6 months	0.48(0.24-0.91)	0.025	0.62(0.32-1.20)	0.153
Type of surgery				

Characteristic	CRR (95%CI)	P-value	ARR (95%CI)	P-value
Phaco	Ref			
ecce	0.68(0.40-1.14)	0.139		
Number of injections				
1	Ref		Ref	
>1	0.38(0.19-0.72)	0.003	0.41(0.21-0.77)	0.006
Vitreous loss				
No	Ref			
Yes	0.72(0.31-1.68)	0.444		
VA at baseline				
≤1logMAR	Ref			
>1logMAR	1.01(0.64-1.60)	0.967		

3.2 Discussion

This study aimed to assess the outcomes and factors associated with intravitreal triamcinolone acetonide (IVTA) injections among Pseudophakic cystoid macular edema patients (PCME) at Kilimanjaro Christian Medical Centre from January 2017 to December 2023.

The current study revealed significant visual improvement following intravitreal triamcinolone acetonide (IVTA) injection among pseudophakic cystoid macular edema (PCME) patients at KCMC, with maximum improvement observed at three months of follow-up. The mean visual acuity in log MAR improved from 1.13(95%CI: 1.02-1.24 SD ±0.51) (snellen cf5m) at baseline to 0.90 (95%CI: 0.80–1.01; SD ±0.48) (snellen 6/60) at one month, 0.78(95%CI: 0.67–0.88; SD ±0.50)(snellen 6/36) at three months, and slightly decreased to 0.80 (95%CI: 0.68–0.91; SD ±0.54) (snellen 6/36) at six months. The findings revealed that IVTA was effective in restoring vision among PCME patients. This may be due to the strong anti-inflammatory effect of triamcinolone acetonide, which reduces vascular permeability and inhibits inflammatory mediators such as prostaglandins and vascular endothelial growth factor. This leads to stabilization of the blood-retina barrier, which facilitates the reabsorption of intraretinal fluid, resulting in visual gain. However, the slight decrease in vision after six months suggests the recurrent nature of PCME after the decline of drug therapeutic level, which usually occurs after 3months post-injection. These results align with (Kuley et al., 2021) and (Hansdak et al., 2021), with similar findings, despite their patients having better baseline visual acuity compared to the current cohort, which accounts for more favorable visual acuity. Another study (Mylonas et al., 2017), (Tariq et al., 2022), and (Dang et al., 2014) also reported visual improvement, followed by slight regression over time.

Regarding anatomical outcome, the mean central macular thickness (CMT) decreased from 498.03 µm (95%CI: 467.95–528.12 µm) at baseline to 325.99 µm (95%CI: 297.97–354.02; p<0.001µm) at three months, followed by slightly increased to 339.74 µm (95%CI: 310.54–368.95µm; p<0.001) at six months. The partial rebound in macular thickness might be due to a decrease in therapeutic drug concentration of triamcinolone in the vitreous cavity, which occurs three to four months post-injection. Furthermore, the chronicity of edema in some patients may hinder the complete resolution despite the treatment. A similar finding has been documented by (Nuwaini et al., 2020), (Kuley et al., 2021), (Hansdak et al., 2021), (Tariq et al., 2022), and (Kasthuribai et al., 2023), who reported a rapid initial drop in macular thickness followed by partial rebound, especially after three months of follow-up.

In the current cohort, only 41.1% achieved a complete success (CMT ≤250µm) by six months of follow-up, showing variability in treatment response. This variation reflects differences in baseline disease chronicity, severity, or systemic comorbidities like diabetes. Nuwaini et al. (2020), found a notable anatomical improvement in diabetic pseudophakic patients, but only 52% patients achieved complete resolution.

The gradual change in anatomical outcome across multiple follow-ups suggests resolution of edema is a gradual process, which emphasizes on close follow-up of patients and the need for re-treatment in case of edema recurrence.

Baseline visual acuity emerged as the strongest independent predictor of visual outcome at six months. Eyes of patients with baseline visual acuity of >1logMAR were 46% less likely to achieve good visual

outcomes, a finding that remained significant in the adjusted relative risk analysis (ARR=0.54; 95%CI: 0.40-0.71; P-value <0.001). This may be due to eyes with poor baseline visual acuity, indicating more chronic and advanced disease, which can lead to irreversible cellular damage and a limited capacity for photoreceptors to recover even after edema resolution. This aligns with the work of (Balasopoulou et al., 2017) and (Sengupta et al., 2018), who reported that patients with good visual acuity at baseline tend to have a favorable prognosis. These results highlight the importance of early detection and timely intervention to prevent irreversible visual impairment.

Although not statistically significant in adjusted relative risk analysis, diabetes patients appeared to have a 22% reduced likelihood of achieving good visual outcomes (ARR=0.78; 95%CI: 0.58-0.10; P-value <0.084) compared to non-diabetic patients. This may be due to underlying microvascular damage, which can hinder visual recovery even after the resolution of macular edema. These findings differ from (Kakkassery et al., 2017), who found no difference between diabetic and non- diabetic patients treated with intravitreal steroid implants. The discrepancy may be due to the small sample size used in this cohort, which limits the generalizability of the results. These observations suggest the need for close monitoring and individualized follow-up in diabetic patients with pseudophakic cystoid macular edema after IVTA injection.

In the current cohort, age, sex, hypertension, surgical type, and number of injections did not show a significant association with visual outcomes.

Older age (above70years) and receiving more than one IVTA were identified as negative predictors of anatomical success. Patients aged 70 years and above were 38% less likely to achieve anatomical success compared to younger individuals (ARR = 0.62; 95% CI: 0.38–0.99; p = 0.045). This may be explained by age-related ocular and systemic changes that compromise the treatment outcomes. With advancing age, the retina undergoes structural degeneration, such as retinal pigment epithelium thinning, which can impair fluid reabsorption and delay the resolution of macular edema. Furthermore, vitreous **syneresis** in older individuals can lead to faster drug dispersion and clearance, thereby reducing drug concentration at the macula, which may limit the therapeutic effects of IVTA. These findings align with those of (Kok et al., 2005) and (Balasopoulou et al., 2017), who reported younger age as a favorable prognostic indicator.

Multiple IVTA injections were significantly associated with a lower likelihood of anatomical success among PCME patients. Individuals who needed more than one injection had 59% (ARR = 0.41; 95% CI: 0.21–0.77; p = 0.006) lower chance of achieving anatomical success than those who received a single IVTA injection. This might be due to a more severe or refractory form of macular edema that does not respond to treatment, or to a tachyphylaxis effect of steroids, whereby by patient responds well to the initial intravitreal triamcinolone injection, but with repeated injection, the sensitivity of the receptors to IVTA decreases. Similar to the study by Chan et al. (2006), which reported comparable findings with the use of multiple IVTA injections in the treatment of diabetic macular edema, these also align with (Wang & Song, 2009), who reported similar outcomes in the treatment of CRVO with the use of 4mg IVTA. The findings suggest that in PCME patients who do not respond to IVTA, an alternative treatment option should be considered.

4 Conclusion

The findings revealed that IVTA is effective in improving both visual acuity and macular thickness in patients with pseudophakic cystoid macular edema. Better baseline visual acuity, younger age, and use of a single injection were significant predictors for successful outcomes. Retreatment should be considered in case of edema recurrence or a decrease in vision. These findings highlighted the need for individualized management among PCME patients, particularly those with poor baseline visual acuity, advanced age, and diabetes.

Study Limitations

Due to its retrospective cohort design, the study is subject to biases related to the quality and completeness of data. However, this design was appropriate because pseudophakic cystoid macular edema is a rare postoperative complication, and a retrospective review enabled the accumulation of a sufficient number of participants that may not have been feasible to recruit in a prospective design. Additionally, the study was conducted in a single center, which may limit the use of these findings to the general population.

Declaration

I declare that I have no financial or personal conflict of interest related to the manufacture, promotion, or distribution of triamcinolone acetonide injection

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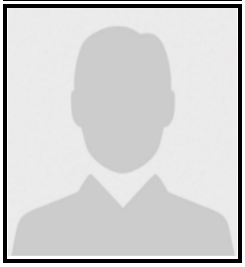

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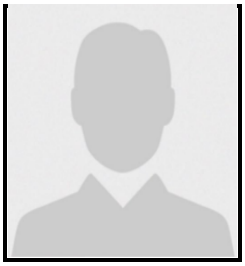

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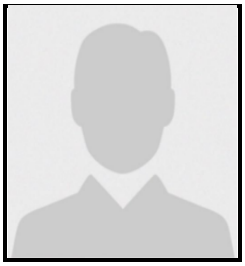

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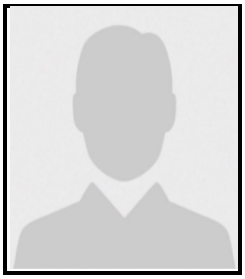

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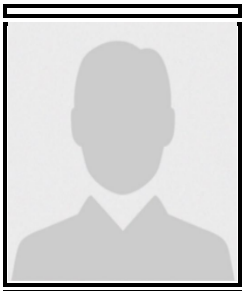

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