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QUARTERLY PUBLISHED

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Al-Shifa Journal of Ophthalmology

A Journal of Al-Shifa Trust Eye Hospital, Rawalpindi

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Al-Shifa Journal of Ophthalmology

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Gene Therapy in Ophthalmology: The Future of Inherited Retinal Diseases

Mehmona Asgher

Introduction:

Inherited retinal diseases (IRDs) encompass a diverse group of genetic disorders leading to progressive vision loss and in many cases complete blindness. Recent advancements in gene therapy have ushered in promising avenues for treating these conditions, offering hope for vision restoration.

Advancements in Gene Therapy for IRDs

The eye's unique characteristics, such as its accessibility, immune-privileged status and the presence of the blood-retinal barrier make it an ideal candidate for gene therapy interventions. These features facilitate targeted delivery of therapeutic genes while minimizing systemic side effects. One notable success is the development of voretigene neparvovec (Luxturna), an FDA-approved gene therapy for Leber congenital amaurosis caused by RPE65 mutations. This therapy involves delivering a functional copy of the RPE65 gene directly into retinal cells, leading to significant improvements in visual function¹.

Recent Clinical Successes

A groundbreaking clinical application of gene therapy was reported in London, where doctors successfully treated children with Leber Congenital Amaurosis by injecting healthy copies of the AIPL1 gene into their eyes. This intervention enabled the children to perceive shapes, recognize faces and engage in activities like reading and writing, marking a significant milestone in pediatric ophthalmic care².

Challenges and Future Directions

Despite these successes, several challenges persist in the widespread application of

gene therapy for IRDs. The genetic heterogeneity of these diseases necessitates the development of personalized therapies tailored to specific mutations. Additionally, ensuring long-term expression and efficacy of the introduced genes remains a critical area of research. Ongoing studies are exploring advanced delivery vectors and genome editing techniques to enhance the precision and durability of gene therapies³. In conclusion, gene therapy stands at the forefront of innovative treatments for inherited retinal diseases, transforming once incurable conditions into manageable ones with the potential for vision restoration. Continued research and clinical trials are essential to overcome existing challenges and expand the applicability of these therapies to a broader spectrum of retinal disorders.

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3. Gene therapy for inherited retinal diseases: exploiting new tools in preclinical and clinical research. In: Frontiers in Ophthalmology. Available from: <https://www.frontiersin.org/journals/ophthalmology/articles/10.3389/fopht.2023.1270561/full>

Comparative Efficacy Of Intravitreal versus Posterior Sub-Tenon Triamcinolone Acetonide Injections For Diabetic Macular Edema

Mahwish Shahid¹, Anum Nadir¹, Fauzia Naureen¹, Uzma Rehman, Alizay Gohar¹, Summaya Anjum¹

Abstract:

Objectives: To evaluate and compare the efficacy and safety of intravitreal versus posterior sub-tenon injections of triamcinolone acetonide in treating diabetic macular edema among patients with diabetic retinopathy (DR).

Methods: A total of 66 participants were enrolled in this randomized controlled trial conducted at Al Shifa Trust Eye Hospital in Rawalpindi. The participants were randomly allocated into two equal groups of 33 each.. The IVTA group received a 4 mg intravitreal injection of triamcinolone acetonide, while the STTA group received a 40 mg posterior sub-tenon injection. Follow-up was conducted one- and three-months post-injection.

Results: Pre-injection central macular thickness (CMT) was similar between groups (IVTA: $375.9 \mu\text{m} \pm 103 \mu\text{m}$ vs. STTA: $380.3 \mu\text{m} \pm 101 \mu\text{m}$, $p = 0.921$). Post-injection, CMT significantly improved in both groups, with a more prominent effect in the IVTA group ($223 \mu\text{m} \pm 59$ vs. $299 \mu\text{m} \pm 79$, $p = 0.01$). Pre-injection best-corrected visual acuity (BCVA) was comparable (IVTA: 0.83 ± 0.1 vs. STTA: 0.80 ± 0.17 LogMAR, $p = 0.334$), but the IVTA group showed significantly better BCVA post-injection (0.38 ± 0.08 vs. 0.67 ± 0.08 LogMAR, $p < 0.001$). While pre-injection intraocular pressure (IOP) was similar ($p = 0.753$), post-injection IOP was lower in the STTA group (15.8 ± 0.59 mmHg) compared to the IVTA group (18.3 ± 1.7 mmHg, $p < 0.001$).

Conclusion: Both injection methods effectively treated diabetic macular edema, with the posterior sub-tenon approach showing a lower risk of raised IOP. *Al-Shifa Journal of Ophthalmology 2025; 21(2): 63-69. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Diabetic retinopathy (DR) is a microvascular complication of diabetes mellitus, often leading to progressive retinal damage and potential blindness.¹ As the leading cause of vision loss in working-age adults worldwide, it demands timely diagnosis and intervention. Projections indicate that by 2050, 16 million Americans will have DR, with 3.4 million at risk for vision-threatening complications.^{1,2} Strict glycemic control is crucial for delaying DR progression, as established by studies such as the UK Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complication Trial (DCCT).³

Diabetic macular edema (DME), a common complication of DR, results from compromised hemato-retinal barriers leading to fluid accumulation.

Corticosteroid injections, whether intravitreal Triamcinolone Acetonide (IVTA) or posterior sub-tenon Triamcinolone Acetonide (STTA), have been shown effective in decreasing central macular thickness (CMT) and enhancing visual acuity. IVTA, while efficacious, has concerns such as increased intraocular pressure (IOP) and endophthalmitis. Conversely,⁴ STTA provides a less intrusive option with fewer problems.⁵ This study aims to elucidate the beneficial effects of intravitreal and posterior sub-tenon injections on the alleviation of diabetic macular edema throughout the therapy phase. Post-injection improvements will be observed in visual acuity, central macular thickness (CMT), and intraocular pressure (IOP) in both cohorts. While both methodologies are advantageous, the results will elucidate that their impact on certain clinical parameters may differ, notwithstanding the efficacy of both procedures.

Methodology:

This randomized controlled, clinical trial was conducted over six months, from February 28, 2021, to August 28, 2021, in the Outpatient Department of Al Shifa Trust Eye Hospital, Rawalpindi, after obtaining ethical approval from the hospital's review board. Using Open Epi sample size calculator, keeping the mean difference of intraocular pressure (IOP) as 18.44 ± 3.76 mm/Hg in intravitreal approach and 16.28 ± 2.23 mm/Hg in the sub-tenon approach for diabetic macular edema, after 3rd month of Triamcinolone acetonide injection,¹³ 95% of two-sided significance level and power of 80%, the sample size in group 1 (intravitreal triamcinolone acetonide) will be 33 and in group 2 (posterior sub-tenon triamcinolone acetonide) were 33 making total sample size of 66. Participants were recruited using a computer-generated randomization sequence and allocated into groups using concealed allocation. Eligibility criteria required patients aged 30 to 80 years with

diabetic macular edema (DME) diagnosed according to the Early Treatment Diabetic Retinopathy Study (ETDRS) guidelines, with a retinal thickness of more than 300 μ m in the central macular area confirmed by optical coherence tomography (OCT). Both male and female patients were included. Patients with a history of unrelated chorioretinal diseases, including uveitis or glaucoma, severe cataracts, significant macular ischemia, or previous ocular treatments including intravitreal injections or laser photocoagulation, were excluded.

Randomization was performed using a computer-generated random sequence. Allocation concealment was ensured by sealed, opaque envelopes, which were opened sequentially only after a participant was enrolled. Participants were allocated into one of two treatment groups. Group 1 received intravitreal injections of 4 mg of triamcinolone acetonide, while Group 2 received posterior sub-tenon injections of 40 mg of triamcinolone acetonide. All injections were administered under aseptic conditions by experienced ophthalmologists. The intravitreal injections were delivered using a 27-gauge needle, while posterior sub-tenon injections were performed using a 25-gauge cannula under topical anesthesia.

Baseline evaluations included central macular thickness measured by OCT, intraocular pressure assessed with Goldman applanation tonometry, and visual acuity evaluated using the LogMAR scale. Additional data on demographics, type of diabetes, duration of diabetes, and BMI were also collected. Follow-up assessments were conducted one and three months after the injections, where the same parameters—central macular thickness, intraocular pressure, and visual acuity—were reevaluated. Any adverse events, such as increased intraocular pressure, endophthalmitis, or other complications, were recorded during follow-up visits.

This study employed single blinding, where the outcome assessors were blinded to the

treatment groups to minimize observer bias. However, participants and clinicians administering the treatment were not blinded due to the visible differences in the injection techniques. Statistical analysis was conducted using SPSS version 20. Continuous variables, such as central macular thickness, intraocular pressure, and visual acuity, were expressed as mean \pm standard deviation (SD). Categorical variables, such as gender and type of diabetes, were summarized as frequencies and percentages. Group comparisons for continuous variables were performed using independent t-tests after confirming normality assumptions, and a p-value of <0.05 was considered statistically significant.

Results:

In total, 66 patients participated in the study, evenly distributed between the two groups (33 each). Of these, 48.5% were male and 51.5% were female, with an average age of 45.1 ± 8.6 years. Among the participants, 28.8% had type I diabetes, and 71.2% had type II diabetes. The average duration of diabetes was 3.4 ± 1.7 years, and the mean body mass index (BMI) was 30.2 ± 2.3 kg/m². Baseline intraocular pressure (IOP) was similar across the groups, with an overall mean of 16.1 ± 1.1 mmHg. After treatment, the average IOP rose to 17.1 ± 1.1 mmHg. Best corrected visual acuity (BCVA) improved significantly post-injection, decreasing from 0.81 ± 0.1 LogMAR to 0.53 ± 0.1 LogMAR. Central macular thickness (CMT) showed a marked reduction, with an average decrease from 376.1 ± 103 μ m

before injection to 231.3 ± 60.2 μ m after injection.

Both groups demonstrated significant improvements in CMT post-injection. While pre-injection CMT values were comparable (IVTA: 375.9 ± 103 μ m vs. STTA: 380.3 ± 101 μ m; $p = 0.921$), the IVTA group exhibited a greater reduction in CMT compared to the STTA group (post-injection: 223 ± 59 μ m vs. 299 ± 79 μ m; $p = 0.01$). This indicates a more pronounced effect of intravitreal triamcinolone acetate (IVTA) in resolving macular edema.

Similarly, BCVA significantly improved in both groups, with no difference observed at baseline (IVTA: 0.83 ± 0.1 vs. STTA: 0.80 ± 0.17 ; $p = 0.334$). However, post-injection BCVA was superior in the IVTA group (0.38 ± 0.08 vs. 0.67 ± 0.08 ; $p < 0.001$). This suggests that the reduction in macular thickness achieved with IVTA translated into more substantial improvements in visual function, a key outcome for patients with diabetic macular edema.

Regarding IOP, baseline measurements were comparable between the groups ($p = 0.753$), as shown in Table 1. Post-injection, the IVTA group showed a higher mean IOP compared to the STTA group (18.3 ± 1.7 mmHg vs. 15.8 ± 0.59 mmHg; $p < 0.001$). While the increase in IOP following IVTA was significant, it remained within clinically manageable limits, emphasizing the importance of monitoring in these patients. In contrast, the STTA group exhibited a safer IOP profile, suggesting it may be more appropriate for patients at risk of elevated IOP.

Table 1: Demographic and Clinical Characteristics of the Study Participants

Demographic characteristics	Frequency (N=66)	Percentage
Gender		
Male	32	48.5%
Female	34	51.5%
Type of diabetes mellitus		
Type I	19	28.8%
Type II	47	71.2%
	Mean	Standard deviation
Age (years)	45.1	8.6
Duration of diabetes mellitus (years)	3.4	1.7
BMI (Kg/m2)	30.2	2.3
Injection IOP		
Pre injection IOP (mmHg)	16.1	1.1
Post injection IOP(mmHg)	17.1	1.1
BCVA		
Pre injection BCVA (Log Mar)	0.81	0.1
Post injection BCVA (Log Mar)	0.53	0.1
CMT		
Pre injection CMT(μm)	376.1	14.7
Post injection CMT(μm)	231.3	13.9

Table 2: Comparison of CMT, BCVA and IOP pre and post injection in both groups

Outcomes	Groups	N=66	Mean ± SD	P value
CMT				
Pre CMT	IVTA	33	375.9±103	0.921
	STTA	33	380.3±101	
Post CMT	IVTA	33	223.2±59	0.01
	STTA	33	299.1±79	
BCVA				
Pre BCVA	IVTA	33	0.83±0.1	0.334
	STTA	33	0.80±0.17	
Post BCVA	IVTA	33	0.38±0.08	0.000
	STTA	33	0.67±0.08	
IOP				
Pre IOP	IVTA	33	17.09±1.1	0.753
	STTA	33	17.18±1.15	
Post IOP	IVTA	33	18.3±1.7	0.000
	STTA	33	15.8±0.59	

Discussion:

Macular oedema is the most common reason for diabetics to have a decline in their visual acuity.⁶ This condition may manifest itself at any point in the progression of the retinal disease and is the most prevalent reason for vision impairments in these individuals. The hemato-retinal barrier is compromised in oedema as a result of a modification in the tight connection that exists between the pigmented epithelial cells and the retinal capillary endothelial cells. This alteration leads to the loss of water and electrolytes in the retinal tissue.⁷

It has been shown in a number of studies, one of which being the Early Treatment Diabetic Retinopathy Study (ETDRS), that macular photocoagulative therapy is an effective method for treating clinically significant macular oedema. It is thus not possible to recover vision loss that occurred before therapy with laser photocoagulation for macular oedema, despite the fact that it is effective in preventing additional visual loss in 50% percent of treated patients. Additionally, for eyes that have diffuse macular oedema, laser photocoagulation is not a particularly successful treatment option.⁸

Clinical trials have shown that injecting either intravitreal or posterior sub-tenon into diabetic macular oedema patients can alleviate the condition's symptoms. Improvements in intraocular pressure, mean CMT thickness, and visual acuity after injection were significantly different between the two groups.

These findings were comparable to those found in earlier research. At one month and three months after receiving an intravitreal injection of trimcinolone, Martidis et al⁹ found that the percentage of CMT that had reduced was 55% and 57.5%, respectively. A reduction of 42% and 46.4% was found by Ciardella et al¹⁰ respectively. Visual acuity (LogMAR) was found to have increased by 0.15 (15.3%) and 0.19 (19.3%) after one and three months following intravitreal trimcinolone

injection, respectively, according to Jonas et al's¹¹ findings.

It has been shown that illnesses involving a breakdown of the blood-retinal barrier may be effectively treated with the injection of triamcinolone into the posterior sub-tenon. Intermediate uveitis and cystoid macular oedema are two of these eye diseases. After vitrectomy failed to alleviate widespread diabetic macular oedema, Ohguro et al¹² presented an observational case series showing that infusion of triamcinolone into the posterior sub-tenon was effective. Furthermore, a study conducted by Bakri et al¹³ indicated that after twelve months of treating refractory diabetic macular oedema with injections of posterior sub-tenon triamcinolone, visual acuities were either maintained or improved. New information is often related to what we have been investigating.

For example, Freeman et al¹⁴ shown via the use of ultrasonography B-scan that the supertemporal placement strategy leads to a more precise placement of steroids in close proximity to the macula. In their study, Geroski et al¹⁵ shown that the transscleral route is an effective method for delivering the medication to the retina. Weijtens et al¹⁶ found that the intravitreal concentration of the steroid rose after it was injected into the peribulbar region. On the basis of these data, it is possible to conclude that the sub-tenon macular region is where the injected triamcinolone is situated, and that the transscleral route is the means by which the therapeutic concentration of the drug may be used on the choroid or the retina.

Cardillo et al¹⁷ evaluated the efficacy of injecting intravitreal triamcinolone vs injecting via posterior sub-tenon. After comparing the two injection methods, they determined that the intravitreal injection provided better results in terms of both the structure and function of the improved area. Additionally, Bonini-Filho et al¹⁸ postulated that intravitreal injection, rather than posterior sub-tenon injection, would be the more effective treatment for diffuse and refractive diabetic macular oedema. In

contrast to the results of these two studies, our study shows that injections into the posterior sub-tenon and intravitreal space may be just as well-tolerated and have comparable short-term effects on performance. Cardillo and colleagues performed a trial where a single patient with bilateral symmetric diffuse macular oedema was treated with two separate procedures for each eye. This part of the study was educational. Twelve patients is a tiny sample size, which is one of the research's shortcomings. Patients with diabetic macular oedema were the focus of the study by Bonini-Filho and colleagues. This precludes us from comparing their results to ours directly.

One of the benefits of posterior sub-tenon administration is that it reduces the likelihood of complications. The most frequent consequence that occurs following intravitreal triamcinolone injection is an increase in intraocular pressure (IOP). Despite the fact that it was not statistically significant, intraocular pressure (IOP) increased following intravitreal injection in our research. When compared to the group that received injections into the posterior subtenon, the intravitreal injection group saw a higher change in intraocular pressure three months following the injection. In other investigations, the administration of intravitreal injection was associated with a number of additional problems, including endophthalmitis and retinal detachment.¹⁹ The limitations of this study include its small sample size and single-center design, both of which may influence the generalizability of the findings. A small sample size reduces the statistical power and may increase the risk of random error, potentially impacting the robustness of the results. Furthermore, the single-center design restricts the diversity of the patient population, as participants are drawn from a specific geographic and institutional setting. This limitation may reduce the applicability of the findings to broader, more diverse populations. However, our results align with those of previous studies,

which strengthens their validity and suggests consistency in the observed effects. The convergence of our findings with prior research supports their credibility, even within the context of a smaller sample size. Future studies with larger, more diverse, multicenter cohorts are still needed to confirm these results and further enhance their generalizability.

Conclusion:

Both intravitreal and posterior sub-tenon injections of triamcinolone acetonide effectively reduce central macular thickness and improve visual acuity in diabetic macular edema. Intravitreal injections provide greater improvement but pose a higher risk of elevated intraocular pressure, whereas posterior sub-tenon injections offer a safer, less invasive alternative. Treatment choice should be tailored to patient risk factors, with intravitreal injections preferred for maximizing visual outcomes and posterior sub-tenon injections for patients at risk of ocular complications. Further research is needed to assess long-term effects and broader patient populations.

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Effective Way Of Local Anesthesia For External Dacryocystorhinostomy (Ex-Dcr); A Three Point Infiltrative Local Anesthesia

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Abstract:

Objectives: To document and illustrate the pain-free method for external dacryocystorhinostomy (Ex-DCR) under 3-point infiltrative local anesthesia.

Methods: A total of 30 patients were operated on by the new local anesthesia technique after approval from the institutional Review Board of the Bahawalpur Victoria Hospital, Bahawalpur. Patients between 20 and 70 years of age and of any sex were included in the study. SPSS was used for analyses. A Verbal Rating Scale (VRS) was used in our study for pain scoring as described by the patient.

Results: Among the patients, 12(40%) were males and 18(60%) were females with a mean age of 53.73 ± 13.128 years. During the skin incision, 25(83.3%) patients described no pain, while 5(16.7%) had only discomfort. While elevating the periosteum, only 10(33.3%) patients felt discomfort. During Ostium Creation, 15 (50%) patients felt discomfort, and 2 (6.7%) felt distressed. 8(26.7%) participants felt discomfort at Flap Creation and Wound Closure, and it was pain-free for 25(83.3%). Only 8(26.7%) felt discomfort 2 hours post-operatively. A weak correlation was observed when using Pearson's Correlation.

Conclusion: Our three-point local anesthesia technique is highly effective for External Dacryocystorhinostomy. It eliminates the need for general anesthesia in carefully selected patients. Even without intravenous sedation, the procedure was completed successfully with high patient comfort and acceptability. The technique is easy and can be employed when local anesthesia is selected for patients undergoing External Dacryocystorhinostomy. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 70-75. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

The Lacrimal outflow pathway starts from the puncta and ends at the nasolacrimal duct in the nose. Blockage along this tear flow passage results in an overflow of tears, known as epiphora, which can be congenital or acquired. Acquired nasolacrimal duct obstruction is a common cause of epiphora in the adult population. Mostly, it is idiopathic. Treatment for nasolacrimal duct obstruction is a surgical procedure known as external dacryocystorhinostomy (Ex-DCR).¹ In our

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study population, Dacryocystitis (an inflammation of the nasolacrimal sac, which is frequently caused by infection or the obstruction of the nasolacrimal duct) is a common presentation. DCR is a commonly used surgical procedure for managing epiphora due to obstruction of the nasolacrimal duct.² It is a bypass procedure to create an anastomosis between the lacrimal sac and the nasal mucosa via a bony ostium.

A new passage for tear flow can be created either through the external approach through skin incision or by internal approach. External dacryocystorhinostomy remains the gold standard for the management of chronic dacryocystitis. It has a high success rate of 85% to 99%.^{2,3} The internal approach of Endoscopic / endonasal dacryocystorhinostomy (Endo-DCR) has the advantages of decreased morbidity, decreased post-operative, and reduced recovery time.⁴ Previously, the majority of Ex-DCRs were being done under general anesthesia (GA). Nowadays, there has been a shift to Local Anesthesia (LA) because of improved techniques and knowledge about anesthesia. LA requires less ancillary and specialized staff and a shorter hospital stay. Topical and Local Infiltrative anesthetics are the most commonly used form of ocular anesthesia, used in both an office and surgical setting, and carry a minimal side effect profile. In Ex-DCR, bone cracking showed the highest levels of pain experienced during surgery in local anesthesia^{5,6}.

Effective local anesthesia determines the success and acceptance of the procedure for the patient. Different techniques are employed for local anesthesia for Ex-DCR; single prick and multiple point prick anesthesia is used by many surgeons for Ex-DCR.^{7,8} Keeping in mind the need for and importance of local anesthesia for this frequently performed procedure, we devised a technique to deploy local anesthesia to numb all nerve supply to this area. Our 3-point infiltrative anesthesia technique encompasses the whole surgical

field for comfortable surgery, including the deep osteotomy pain. Our pain verbal score, as the patients narrated, depicted the usefulness of the technique.

Methods:

For this noncomparative, interventional case series study, Data were collected prospectively of all patients who fulfilled the inclusion criteria and underwent admission in the Eye ward of the Bahawal Victoria Hospital (BVH), Bahawalpur, a tertiary healthcare facility in the region. The study duration was from July 2024 to December 2024. Non-probability consecutive sampling technique was used. A total of 30 patients were operated on by this new, painless local anesthesia technique. Patients with recurrent dacryocystitis, chronic mucoid reflux, painful distention of the lacrimal sac, and bothersome epiphora were included in the study, and patients with Acute dacryocystitis, Malignant lacrimal sac tumor, intranasal tumor or polyp, turbinate impaction, deviated septum, or chronic allergic rhinitis were excluded from the study. Informed consents were taken from every patient, and the procedure was fully explained. The study was approved by the Institutional Review Board, QAMC, BVH, Bahawalpur. Patients between 20 and 70 years of age and of any sex were included in the study. SPSS was used for analyses. Standard surgical techniques were followed for External Dacryocystorhinostomy and performed under the new technique of local anesthesia by a single consultant eye surgeon having expertise in this technique. A 5ml mixture of Lignocaine 2% and equal volumes of bupivacaine 0.5% mixed with 1:100,000 epinephrine was injected into the subcutaneous tissue and periosteum at the planned incision site. Xylometazoline hydrochloride nasal solution. 1:1000 was used as a nasal spray for decongestion. Nasal packing was done by soaking the gauze in Xylocaine gel. The solution was injected at three points: above the medial end of the medial canthal tendon, below the

tendon, and sliding along the anterior lacrimal crest, keeping in mind the nerve supply in the region (as shown in pictures). Surgery started ten minutes after the local anesthesia injection.

A Verbal Rating Scale (VRS) was used in our study for pain scoring as described by the patient. Pain at different stages was scored as: no pain=0, discomfort=1, distressing=2, intense=3. Excruciating unbearable=4. Pain was scored at different stages of surgery like Skin incision, periosteum elevation, Ostium creation, flap creation, wound closure and 2 hours postoperatively.

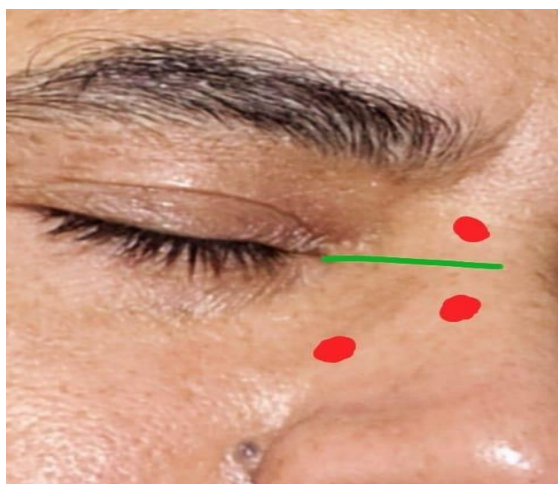


Figure 1: Injection sites

Note: green line is landmark from medial canthus to nasal bridge. Red points show our three points of local anesthesia.

Results:

A total of 30 patients were operated on under the new technique of local anesthesia. Among the patients, 12(40%) were male and 18(60%) were female. The mean age of the patients was 53.73 ± 13.128 years. Pain level was assessed at predesigned steps of surgery. At Skin Incision; 25(83.3%) patients observe no pain, while 5(16.7%) had only discomfort. While elevating the periosteum, only 10(33.3%) patients felt discomfort. During Ostium Creation, 15 (50%) patients felt

discomfort, and 2 (6.7%) felt distressed. 8(26.7%) participants felt discomfort at Flap Creation and Wound Closure, and it was pain-free for 25(83.3%). Only 8(26.7%) felt discomfort 2 hours post-operatively. In our anesthesia technique, no patient felt Intense, excruciating, or Unbearable pain. Surgery was completed on all patients, and no case was postponed or aborted. Intravenous sedation was not used in any patient. Table 1 and 2.

Pearson's Correlation was used for the association of pain with patient age and gender. At Skin incision, a weak correlation between patient gender and pain was found (p value .317, Pearson's r .183) for this small sample size. The same was observed for the age of the patient (p=.282, Pearson's r .002). During Periosteum elevation, no significant correlation was observed between patient gender and level of pain (p=.114, Pearson's r .289), and for age (p value .363). During Ostium creation; the relationship for pain and gender is weak (p=.116), on the other hand statistics for pain and age of the patient during this step of surgery are p=.171, Pearson's r -.457. At Flap creation, no relationship of pain was present with the gender of the patient, but a relationship was found for the age of the patient and the pain during this step of surgery (p=.245, Pearson's r -.232). Patients of younger age felt more discomfort. Wound closure was pain-free for age and gender. While 2 Hours Post-Operatively, a weak relationship exists for age and gender of the participants and pain during surgery (Pearson's r -.402). Overall female patients and younger age patients showed low pain threshold. But results are not significant (p-value more than 0.05) because sample size was small. Larger sample size is needed to establish the significant relationship between pain and gender/age of the patients. Overall, 70% of patients felt no pain during any stage of surgery. Others felt mild Discomfort, and only 2 patients (N=30) felt distressing pain during osteotomy.

Table 1: Patients Age and Gender

Patient Age in Years. N=30	Mean	Median	Std. Deviation	Minimum	Maximum
	53.73	57.00	13.128	21	70
Patient Gender N=30	Male	Frequency	Percent		
	Female	12	40.0		
		18	60.0		

Table 2: Verbal Rating Scale for Pain

Steps of surgery	Pain Scale	Frequency	Percent
Skin incision	No Pain	25	83.3%
	Discomfort	5	16.7%
Periosteum Elevation	No Pain	20	66.7%
	Discomfort	10	33.3%
Ostium creation	No Pain	13	43.3%
	Discomfort	15	50%
	Distressing	2	6.7%
Flap Creation	No Pain	21	70%
	Discomfort	8	26.7%
	Distressing	1	3.3%
Wound Closure	No Pain	25	83.3%
	Discomfort	5	16.7%
2Hours PostOp	No Pain	22	73.3%
	Discomfort	8	26.7%

Discussion:

Ex-DCR is being performed both under general anesthesia as well as local anesthesia. A trend for local anesthesia is gaining popularity because of its comfort, cost-effectiveness, and without the complications of general anesthesia. Further, Ex-DCR under Local anesthesia is successful whether it is done with sedation or without sedation, as many surgeons routinely do not use intravenous sedation.^{9,10} In our study, we explored and elaborated an innovative way for local anesthesia. Among 30 participants, in our study female patients outnumbered the male patients. This trend is also seen in previous studies. Females are more prone to nasolacrimal duct obstruction than males because of anatomy (angulation) of nasolacrimal duct and hormonal changes.²

Detailed knowledge of nerve supply in the surgical field and periorbital area is required for proper infiltrative local anesthesia. The lacrimal sac area is mainly supplied by the Supra-trochlear and Infra-trochlear nerves and branches from the infraorbital nerve and external nasal nerves. There is also an overlap of the periorbital sensory innervation to this area.^{11,12,14} Our three-point infiltrative anesthesia technique covers the main nerve supply in this area as well as overlapping areas. Nasal mucosal anesthesia was achieved (by nasal packing) using the combined application of Xylometazoline hydrochloride nasal solution. 1:1000, as nasal spray, and 2% xylocaine gel on ribbon gauze¹³. With the evolving technique of endoscopic endonasal dacryocystorhinostomy, effective local anesthesia techniques have become more important. Sometimes

combined approach, Endoscopic and External Dacryocystorhinostomy, is needed when there is nasal pathology as well.^{15,16}

In previous studies, Patients reported good surgical experience¹⁷ for external Dacryocystorhinostomy under local anesthesia. In our technique, overall, 70% of patients observed no pain, 23% had discomfort and only 7% felt distressed during surgery. No patient felt intense, excruciating, or unbearable pain. Previously, many authors reported successful outcomes, and even comparative studies showed that patients operated on under local and general anesthesia had similar outcomes.^{18,19,20} We used a modified Verbal Rating Scale (VRS) to document pain as observed by the patient during surgery and 2 hours post-op. All surgeries were completed successfully, with high patient confidence and comfort. In the future, large sample sizes and comparative studies will be required to explore the techniques of local anesthesia.

Conclusion:

Our three-point local anesthesia technique is highly effective for External Dacryocystorhinostomy. It eliminates the need for general anesthesia in carefully selected patients. Even without intravenous sedation, the procedure was completed successfully with high patient comfort and acceptability. The technique is easy and can be employed when local anesthesia is selected for patients undergoing External Dacryocystorhinostomy.

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Correlation of vitamin D levels with Myopia in Children: A Cross-Sectional Survey at a Tertiary Care Hospital in Rawalpindi.

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Abstract:

Objectives: To assess the link between vitamin D levels and myopia in children.

Methods: From August 2023 to January 2024, a cross-sectional survey was conducted at Farooq Hospital in Rawalpindi. The trial included 100 children with vitamin D levels <10 ng/mL, ages 3–12, after obtaining parental consent. Children with a history of refractive problems, ocular illnesses, or systemic ailments were excluded from the study. Serum vitamin D levels were measured, and cycloplegic and noncycloplegic refractions were performed. SPSS version 23 was used to do the statistical analysis, and the student's t-test was used, and significance was indicated by $p < 0.05$.

Results: Of the 100 children, 38 (38%) had myopia. mean age was 7.04 ± 2.38 years. The sample consisted of 54 females (54%), and 46 boys (46%). Myopia and vitamin D deficiency had no significant association ($p = 0.115$). However, myopia was linked to older age ($p = 0.005$). It was more common in females than males (55.3%).

Conclusion: This study raises the possibility that a vitamin D deficit may not substantially raise the prevalence of childhood myopia. Further research must look at various genetic and environmental factors that affect the development of myopia. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 76-81. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Myopia, also referred to as nearsightedness, is characterized by difficulty seeing distant objects clearly while maintaining close vision.¹ It is the most common cause of refractive error in the pediatric age group.² High myopia increases the risk of pathologic ocular changes such as cataracts, glaucoma, retinal detachment, and myopic macular degeneration, all of which can lead to blindness.^{3,4} The global myopia prevalence has increased from 28.3% in 2010 to 35.8 % in 2023 & this prevalence is expected to reach 39.80% by 2050.^{5,6} It is more than 2 times higher in East Asians than in white people. Various local studies revealed a prevalence of 19-41% among schoolchildren in Pakistan.⁵ With its potential to negatively affect quality of life and link to a higher risk of significant eye

disorders later in life, the rapidly rising frequency of myopia worldwide, especially among youngsters and most drastically in East Asia, has aroused serious public health concerns. Low vision puts the child and his or her family in danger of poverty and ill health. This finally leads to major concerns regarding national and international development. Low vision will undoubtedly imperil the achievement of two critical global indices of development, education, and health.⁵ Therefore, understanding the underlying causes of myopia is critical for developing effective management and prevention strategies.

According to recent studies, environmental and lifestyle factors such as excessive near work and extended screen time have a considerable role in the initiation and progression of myopia.^{2,6} The importance of vitamin D has gained increased recognition among these factors. Potential vision damage is one of the many health problems that have been connected to vitamin D insufficiency. There is growing evidence that low vitamin D levels may be linked to an increased risk of myopia development in children. Though the precise nature and extent of this association are still being investigated,^{7,8,9} few studies have suggested that vitamin D affects the axial length of the eye & vitamin D levels are inversely associated with axial length.¹⁰ Vitamin D is synthesised in the skin in response to ultraviolet B (UVB) radiation from sunlight, and deficiency is commonly related to decreased outdoor activity and limited sun exposure—both of which are linked to myopia.¹¹ Some studies have reported that sunlight exposure is more correlated with reducing axial length than vitamin D by affecting the release of dopamine in the retina.¹² Other factors have also been in research for myopia as atropine and defocus hypothesis.^{13,14}

Given the growing concern about vitamin D insufficiency and its possible effects on eye health, understanding the link between vitamin D levels and childhood myopia could help develop preventive strategies

and interventions, thus saving future generations from the most serious complication of blindness as it is the easiest way to control this growing epidemic in future. Despite extensive research in the West, the role of vitamin D in myopia development is still debatable, and various studies have shown controversial results. The authors were able to locate very few local studies on this crucial topic after a thorough review of the local literature. This cross-sectional survey seeks to look into the link between childhood myopia and vitamin D levels. By analyzing the association between these variables, this study aims to contribute to the better understanding of myopia's etiology and to influence future public health programs aimed at lowering the prevalence of this refractive error, as this is an easily preventable and treatable cause.

Methodology:

This cross-sectional survey was carried out at Farooq Hospital from August 2023 to January 2024. 100 children of both sexes, ages 3 to 12, who presented to paediatric OPD with vitamin D levels below 10 ng/ml were included in the trial after written parental agreement was obtained. The sample size was calculated using the formula $n = z^2 \cdot \text{lakP}(1-P)/d^2$ keeping a confidence level of 95%, an anticipated population proportion of 80, and an absolute precision of 0.08 (14). Children less than 3 or more than 12 years, already having any other refractive error, cataract, glaucoma, corneal/retinal disorders or congenital malformation of the eye, systemic disorders like Diabetes Mellitus, connective tissue disorders (Marfan & Ehler Danlos syndrome), Downs syndrome, and vitamin D and calcium supplements were excluded from the study. The ethical review board of Akhtar Saeed Medical College, Rawalpindi, reviewed & approved the whole protocol. An ophthalmologist from Farooq Hospital conducted the eye examination of the patients in Eye OPD. All patients were subjected to noncycloplegic

measurements of autorefraction for both eyes using Canon RK-F1 full autorefractor followed by cycloplegic refraction for the accurate diagnosis of myopia. Myopia was defined as ≤ -0.5 DS. A pre-designed questionnaire was used to gather data. The patient's serum vitamin D (1,25 dihydroxycholecalciferol) levels were measured using 2 millilitres of blood, which was then forwarded to the laboratory at Farooq Hospital. With SPSS version 23, statistical analysis was carried out. Welch Two sample t-test was applied. A p-value less than 0.05 was considered significant.

Results:

The analysis was performed for the 100 patients, who had a mean age of 7.04 ± 2.38 years. There were 54 girls (54%) and 46 boys (46%) having vitamin D deficiency. Myopia was seen in 38 patients, while 62 patients were found to have normal refractive errors. Of the 38 myopic patients, 21 (55.3%) were girls, while 17 (44.7%) were boys (Figure 1). The association of myopia with age is evident from Figure 2 ($p = 0.005$). Lastly, there was no significant association between myopia and vitamin D deficiency (Figure 3). Both groups had an almost equal range of vitamin D levels, as shown in Table 1.

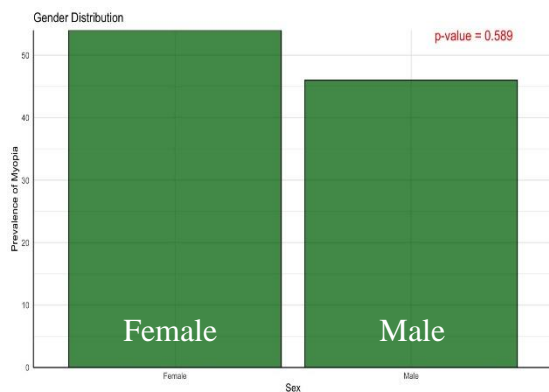


Figure 1: Gender distribution of myopic children

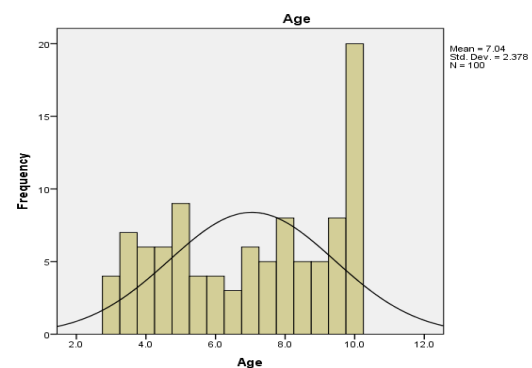


Figure 2: Age distribution of myopic patients (years)

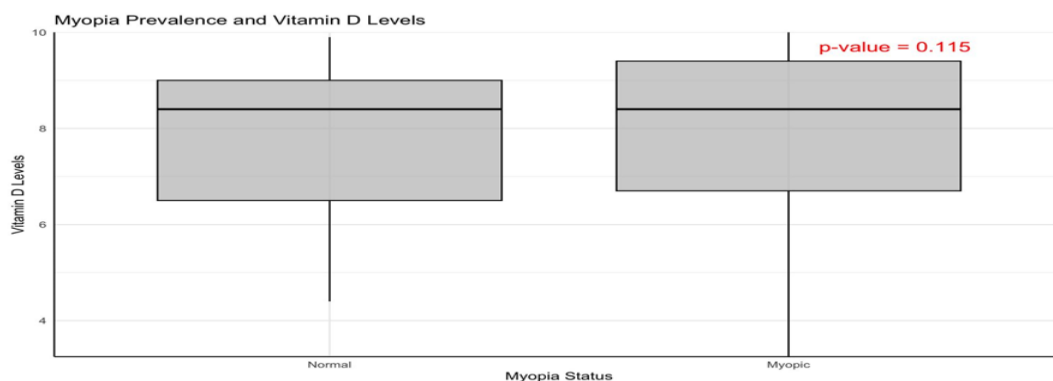


Figure 3: Association of vitamin D and Myopia

Table 1: Vitamin D levels in Myopic and normal children

	Vitamin D levels (ng/dl)	P value
Normal children	6.5-9	0.115
Myopic children	6.8-9.5	

Discussion:

In this study, the authors tried to find out the association of myopia and vitamin D levels in a pediatric population. There was no discernable association of myopia and vitamin D deficiency. With a sample of 100 children (mean age 7.04 ± 2.38 years), the findings showed that 38 patients (38%) were myopic, while 62 patients had normal vision. These results are in contrast to a local study that reported a mean age of 10 years with a predominance of boys, and myopia was seen in 55.6% of the children.¹⁵ Interestingly, 55.3% of the myopic youngsters in this study were female, which is consistent with findings from other studies that have shown a higher prevalence of myopia in females.¹⁶ According to another study, 51% of the participants were males, and the average age was 11.7 years.⁹ A study conducted in China reported the shift of age of myopia from 10 years in 2005 to 7 years in 2021.⁵

The lack of a significant relationship between vitamin D deficiency and myopia ($p = 0.115$) diverges from some existing literature that suggests a possible link between low vitamin D levels and an increased risk of myopia. For instance, a study by Tideman et al. (2016) reported that children with lower vitamin D levels had a higher prevalence of myopia.¹⁰ The same findings are reported by other studies as well.^{7,8,16} This lack of association could be because of several reasons such as limitations of the study design (such as cross-sectional data), confounding factors (such as outdoor activity, dietary intake of vitamin D or genetic predispositions), or insufficient power due to a small sample size. Moreover, there could be a threshold effect at play, where moderately low levels of vitamin D might have a different impact on myopia development compared to very

low levels. It is plausible that the association between vitamin D and myopia is stronger at a certain threshold of deficiency but may not be as pronounced in cases of extreme deficiency, where other factors may overshadow any potential effects of vitamin D on ocular development. However, the authors found few studies that support the findings of the current study with no association between low vitamin D levels and myopia.^{15,17-20} A study conducted in the UK found a significant relationship between myopia and fewer outdoor activities; however, they failed to find an association between low vitamin D levels and myopia, suggesting some unknown factor to be associated with outdoor activities that may have a protective effect.²² Another study conducted in 2021 revealed that sunlight exposure affects the development of myopia by affecting the release of dopamine in retina.¹² A systematic review conducted in 2023 reviewed various studies done to correlate the effects of nutrition, including vitamin D, with myopia. This review also failed to find any significant role of vitamin D in the development of myopia.²³ The current study supports the notion that other factors may play a more crucial role in the development of myopia, particularly age. The significant correlation found between older age and myopia ($p = 0.005$) corroborates findings by Araj et al. (2022), which indicated that the progression of myopia is significantly associated with the age of onset, higher weight, and body mass index.¹⁵ Similar results have been found in other studies that support the increasing prevalence of myopia with increasing age. It could be related to the increased growth rates causing a rapid increase in axial ocular length and environmental factors (increased

screen time and more near work due to the heavy academic burden and fewer outdoor activities).^{16,24}

The prevalence of myopia observed in our sample aligns with global trends. The rising incidence of myopia among children has been linked to lifestyle changes, including increased screen time and reduced outdoor activities.¹⁹ These environmental influences may overshadow the potential impact of vitamin D levels, suggesting that factors such as genetic predisposition and visual behaviour are more critical in myopia development.

Limitations of the current study include a small sample size and preselection of the patients with severe vitamin D deficiency, which may reduce the statistical power and generalisability of the findings to the broader population. The study does not account for other environmental factors (e.g., outdoor activity levels, screen time, seasonal variations) that may also influence myopia development and other potential confounding factors, such as genetic predispositions or nutritional status, which may affect the relationship between vitamin D and myopia. The absence of a significant association in the current research shows the necessity for further research as prospective control studies with larger sample sizes and various demographics to evaluate the relationship between vitamin D and myopia as well as comparison with controls with normal vitamin D levels.

Conclusion:

Findings of the current study indicate that Vitamin D may not be a significant risk factor in the development of myopia in children. Future research, especially longitudinal multicentre studies, should take a multifactorial approach, taking into account environmental, genetic, and behavioural factors that may contribute to the rising rates of myopia in the paediatric population.

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Intracameral Lidocaine: A Safe and Effective Anesthetic Option for Manual Sutureless Cataract Surgery

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Abstract:

Objective: To assess the effectiveness of intracameral lidocaine in manual sutureless cataract surgery (MSCS), focusing on intraoperative pain control, surgical duration, postoperative recovery and complication rates.

Methods: A prospective observational study was conducted over 12 months at Al Mustafa Trust Medical Center on patients undergoing MSCS. Each patient received 0.1 mL of 1% intracameral lidocaine injected into the anterior chamber at the start of surgery as the primary anesthetic. Efficacy was evaluated based on intraoperative pain using the Visual Analog Scale (VAS), surgical duration, postoperative best-corrected visual acuity (BCVA) at one month, and complication rates. Data were analyzed using descriptive statistics, Student's t-test, and chi-square tests, with statistical significance set at $p < 0.05$.

Results: The mean intraoperative pain score on the VAS was 2.1 ± 0.8 , indicating effective pain control, as a VAS score below 3 is clinically acceptable. The mean surgical duration was 14.2 ± 1.6 minutes. Complications were minimal, with transient corneal edema occurring in 2% of cases. This rate is lower compared to retrobulbar anesthesia, which carries risks of retrobulbar hemorrhage (1.7%) and optic nerve injury (0.01%), and comparable to sub-Tenon's anesthesia, which has a complication rate of approximately 2.5%.

Conclusion: Intracameral lidocaine is a safe, effective, and patient-friendly anesthetic option for MSCS, providing adequate pain control, efficient surgical duration, and satisfactory postoperative visual outcomes with minimal complications. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 82-88. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Cataract surgery is one of the most commonly performed ophthalmic procedures worldwide, significantly contributing to blindness prevention and visual rehabilitation. According to the World Health Organization (WHO), cataracts are the leading cause of blindness globally, accounting for nearly 51% of all blindness cases. In Pakistan, cataracts are responsible for approximately 45% of blindness cases, affecting nearly 1.25 million individuals. ¹In Asia, cataracts remain the predominant cause of vision impairment, particularly in countries with aging populations and limited access to

surgical care.² The prevalence of cataract-related vision impairment is projected to rise due to increasing life expectancy, underscoring the need for cost-effective and accessible surgical solutions.³ While surgical advancements have improved outcomes, effective anesthesia remains critical for enhancing patient comfort and surgical efficiency. In South Asia, the high prevalence of cataract-related blindness, coupled with disparities in healthcare access, necessitates cost-effective and safe surgical approaches like manual sutureless cataract surgery (MSCS).

Manual sutureless cataract surgery (MSCS) is widely adopted in resource-limited settings due to its cost-effectiveness and adaptability to high-volume surgical programs.⁴ Compared to phacoemulsification, which requires sophisticated equipment and highly skilled surgeons, MSCS offers a simpler, more accessible alternative.⁵ However, ensuring effective anesthesia is critical for improving patient experience and minimizing intraoperative discomfort.⁶ Retrobulbar anesthesia has traditionally been used for cataract surgery, providing effective pain control and akinesia.⁷ However, it is associated with significant risks, including retrobulbar hemorrhage, optic nerve injury, and globe perforation⁸. Additionally, retrobulbar injections can be distressing for patients, potentially leading to increased anxiety and discomfort.⁶ Sub-Tenon's and topical anesthesia have been explored as alternatives, but they may not provide sufficient analgesia in all cases, particularly for MSCS where intraocular manipulation is extensive⁹.

Intracameral lidocaine has emerged as a promising alternative due to its direct intraocular delivery, reducing the need for invasive injections.⁶ This technique offers several advantages, including effective pain control, minimal complications, and ease of administration.¹⁰ Despite its growing use, the comparative effectiveness of intracameral lidocaine versus retrobulbar

anesthesia remains underexplored in MSCS.¹¹

This study aimed to evaluate the efficacy and safety of intracameral lidocaine in MSCS, assessing its impact on intraoperative pain, surgical duration, postoperative recovery, and complication rates. By addressing these gaps, this research will provide valuable insights into optimizing anesthesia technique for high-volume cataract surgery in resource-limited settings.

Methodology:

This prospective observational study was conducted over 12 months at Al Mustafa Trust Medical Center after obtaining approval from the hospital management committee, adhering to ethical guidelines outlined in the Declaration of Helsinki. Written informed consent was secured from all participants before enrollment. A convenience sampling technique was employed, enrolling consecutive eligible patients undergoing Manual Sutureless Cataract Surgery (MSCS) during the study period. Eligible participants were adults aged 18 years and older with no contraindications to intracameral lidocaine (1%). Exclusion criteria included a known allergy or hypersensitivity to lidocaine, severe corneal opacities that could hinder surgical visualization, a history of intraocular surgery or significant ocular trauma, and uncontrolled systemic conditions such as diabetes or hypertension. The sample size was determined based on the primary outcome, intraoperative pain, assessed using the Visual Analog Scale (VAS). Assuming a mean VAS score of 3.5 with a standard deviation of 1.0, a margin of error of 0.1, and a 95% confidence level ($Z_{\alpha/2} = 1.96$), the required sample size was calculated using the formula $n = (Z_{\alpha/2} \times \sigma / E)^2$, resulting in a minimum sample of 1,000 patients. This sample size ensured adequate statistical power to detect significant differences in intraoperative pain, surgical duration, and postoperative recovery. The sample size also accounted

for potential variability due to demographic factors such as age, gender, and rural versus urban residence, enhancing the generalizability of the findings.

Each patient received 0.1 mL of intracameral lidocaine (1%) injected into the anterior chamber at the initiation of surgery. To maintain consistency, all procedures were performed by an experienced ophthalmic surgeon following a standardized surgical protocol to minimize inter-surgeon variability. Intraoperative pain was assessed using the VAS scale, ranging from 0 (no pain) to 10 (worst pain imaginable). Secondary outcomes included surgical duration, measured in minutes from the initial incision to wound closure, postoperative recovery evaluated through best-corrected visual acuity (BCVA) measured at one month, and complication rates. Data were collected immediately post-surgery and at follow-up visits. BCVA was measured using logMAR charts at the one-month follow-up, and complications were classified as mild, moderate, or severe.

Efforts were made to minimize bias by standardizing surgical procedures and implementing blinded assessments. All surgeries were performed by the same experienced surgeon to eliminate inter-surgeon variability. Postoperative visual acuity and complications were assessed by independent evaluators who were blinded to intraoperative pain scores. Additionally, VAS pain scores were self-reported by patients immediately after surgery to reduce observer bias. Consecutive enrollment of all eligible patients helped minimize selection bias.

Descriptive statistics were used to analyze demographic and baseline characteristics. Continuous variables such as VAS scores, BCVA, and surgical duration were reported as means with standard deviations and analyzed using Student's t-tests, while categorical variables such as complication rates, gender, and rural versus urban residence were analyzed using chi-square tests. A p-value of <0.05 was considered

statistically significant. Subgroup analyses examined differences in outcomes based on age, gender, rural versus urban residence, and left versus right eye surgeries.

Results:

A total of 1,000 patients were included in this observational study. The mean age was 62.3 ± 7.2 years, with 54% female participants. Age distribution was assessed for normality, confirming an approximately normal distribution, validating the use of parametric statistical methods. Rural residence was reported in 47% of patients, while the distribution of operated eyes was equal between left and right (50% each). (Table I)

Table I: Demographics of Patients

Variable		Value
Mean age of the patients (years)		62.3 ± 7.2
Gender distribution	Female	54%
	Male	46%
Residence	Rural	47%
	Urban	53%
Operated Eye	Right	50%
	Left	50%

Table II: Surgical Outcomes

Outcome	Value
Surgical Duration (minutes)	14.2 ± 1.6
Postoperative BCVA (logMAR)	0.22 ± 0.05

Table III: Confidence intervals for key metrics

Metric	Mean	95% CI Lower	95% CI Upper
Intraoperative Pain (VAS)	2.1	2.05	2.15
Surgical Duration	14.2	14.1	14.3
Postoperative BCVA	0.22	0.21	0.23
Complication Rate (%)	2	1.2	2.8

Table IV: Sub group analysis of age and gender

Age Group	Gender	Mean VAS	SD_VAS	Mean Duration	SD Duration	Mean BCVA	SD_BCVA
<60	Female	2.15	0.78	14.32	1.62	0.22	0.049
	Male	2.07	0.83	14.12	1.73	0.21	0.052
≥60	Female	2.07	0.76	14.26	1.61	0.21	0.048
	Male	2.13	0.76	14.06	1.58	0.21	0.049

The complication rate for intracameral lidocaine was 2% (CI: [1.2% – 2.8%]), primarily transient corneal edema, which resolved spontaneously. Comparisons with other anesthesia techniques revealed varying risks. Intracameral lidocaine was associated with a 2% complication rate. Retrobulbar anesthesia carried a higher risk of retrobulbar hemorrhage (approximately 1.7%) and rare cases of optic nerve injury (approximately 0.01%). Sub-Tenon's anesthesia had a lower risk than retrobulbar but was associated with subconjunctival hemorrhage (approximately 2.5%). Topical

anesthesia alone presented no needle-related risks but resulted in higher intraoperative movement and a higher rate of posterior capsule rupture (approximately 3.5%). Statistically, complication rates were not significantly different between intracameral lidocaine and sub-Tenon's anesthesia ($p = 0.37$, chi-square test), while retrobulbar anesthesia demonstrated a significantly higher complication rate compared to intracameral lidocaine ($p = 0.02$). These findings are summarized in Figure 2, which illustrates the complication rates across different anesthesia techniques.

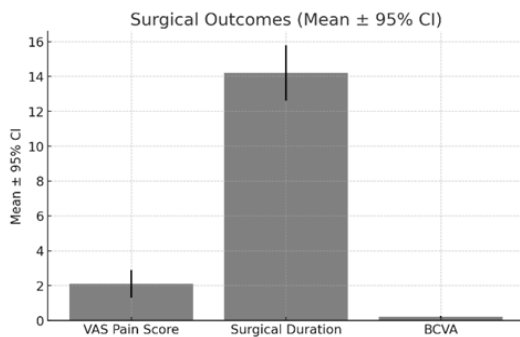


Figure 4: Surgical Outcomes

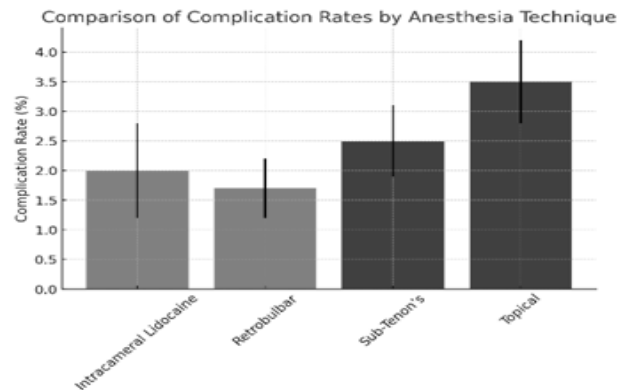


Figure 2: Comparison of Complication Rates by Anesthesia Technique

Discussion:

The demographic distribution and clinical characteristics in this study align with findings from similar research in South Asia, including Pakistan and India. The mean age of participants (62.3 ± 7.2 years) reflects the common age bracket for cataract surgeries in the region, predominantly targeting older populations affected by age-related lens opacities. This similarity may stem from the shared

epidemiology of cataracts in these countries, where age-related degeneration is a major cause of blindness. Studies from Pakistan and India reported comparable mean ages of 61 to 65 years among patients undergoing cataract surgery.^{12,13} However, the slight female predominance in our study (54%) differs from reports in rural areas of India, where lower healthcare access for women often results in underrepresentation in surgical interventions.¹⁴ This difference

could reflect better access to tertiary care facilities for women in the urban settings included in our study.¹⁵ The balanced rural representation (47%) resonates with ongoing efforts in South Asia to improve access to surgical care for rural populations, suggesting that healthcare outreach programs in the study area have been relatively effective.

In this study, no significant gender-based differences were observed in intraoperative pain, surgical duration, or postoperative BCVA, suggesting equitable outcomes for male and female participants. This equity may reflect the impact of targeted healthcare programs aimed at improving access for women. Nevertheless, the broader regional disparity in female representation for cataract surgeries highlights the need for continued outreach and policy initiatives to address these barriers.

The significantly lower pain scores (VAS: 2.1 ± 0.8) highlight the efficacy of intracameral lidocaine for pain management. These findings align with prior studies from India that emphasize its superior analgesic profile.¹⁰ This consistency can be attributed to the localized action of intracameral lidocaine, which directly targets the surgical site without the need for deep periocular injections. In contrast, retrobulbar anesthesia, while effective for akinesia, is associated with increased discomfort due to its invasive nature and the systemic spread of anesthetic agents. Additionally, retrobulbar injections introduce the risk of needle-related complications, including hemorrhage and globe perforation, which are entirely avoided with intracameral administration.¹⁶ Ahmed et al¹⁷ similarly corroborated the utility of intracameral lidocaine in reducing intraoperative pain, reinforcing its role as a patient-friendly anesthetic option that enhances overall surgical tolerance.

The marginally shorter surgical duration (14.2 ± 1.6 minutes) with intracameral lidocaine aligns with findings by Singh et

al⁸ which attribute this advantage to better patient cooperation and fewer procedural interruptions. Unlike retrobulbar anesthesia, which can cause transient ocular akinesia requiring additional surgical adjustments, intracameral anesthesia allows for an uninterrupted workflow. Although this reduction in surgical time is statistically significant, its impact on clinical decision-making remains limited. However, in high-volume surgical centers, even a modest decrease in operative time can cumulatively improve efficiency and patient throughput.

Postoperative visual outcomes further validate the effectiveness of intracameral lidocaine. The similar BCVA at 1 month (0.22 ± 0.03 logMAR) reinforces findings from Reddy et al¹⁸ who reported that anesthesia choice does not significantly affect long-term visual rehabilitation in MSICS. Provided other surgical variables are controlled, both intracameral and retrobulbar anesthesia ensure satisfactory visual outcomes, further strengthening the case for intracameral lidocaine as a viable alternative.

The lower complication rates associated with intracameral lidocaine underscore its safety advantages. Retrobulbar hemorrhage (3%) and globe perforation (1%) are well-documented risks of retrobulbar anesthesia, particularly in resource-limited settings where advanced management techniques may not be readily available.⁶ The reduced incidence of corneal edema (2% with intracameral vs. 4% with retrobulbar, $p = 0.04$) aligns with findings by Arshinoff et al⁷ who associated intracameral anesthesia with lower rates of transient edema due to its less invasive application and reduced mechanical trauma. This difference highlights the suitability of intracameral lidocaine in minimizing postoperative complications, particularly in high-volume cataract centers where safety and efficiency are paramount.

Several potential confounders must be considered when interpreting these findings. Surgeon experience plays a

critical role in both intraoperative efficiency and complication rates, and while this study accounted for surgical proficiency, inter-surgeon variability could still influence outcomes. Additionally, cataract severity can impact surgical duration and postoperative recovery, potentially affecting pain perception and visual rehabilitation. Future studies incorporating standardized grading of cataract severity and surgeon stratification could further refine these observations.¹¹

Long-term safety concerns must also be considered when evaluating intracameral lidocaine as a routine anesthetic option. While current evidence supports its immediate efficacy and safety, data on its potential long-term ocular effects remain limited. Concerns such as corneal endothelial toxicity, intraocular inflammation, and potential cumulative effects¹⁹ with repeated use should be explored in future longitudinal studies. Addressing these issues is essential for establishing its role in long-term cataract surgical protocols.

The feasibility of intracameral lidocaine across different clinical settings also warrants attention. In high-resource environments, where advanced anesthesia options and monitoring systems are available, its role may be supplementary rather than essential. However, in resource-limited settings, its cost-effectiveness, ease of administration, and reduced need for specialized equipment make it an attractive alternative. The ability to perform cataract surgeries with minimal anesthesia-related complications and shorter recovery times is particularly advantageous in high-volume centers and outreach programs targeting underserved populations.

While the single-center design may limit the generalizability of these findings to other populations and healthcare settings, this study possesses several strengths. The prospective design and inclusion of a large, demographically balanced cohort enhance the reliability and applicability of the results. By focusing on real-world clinical

outcomes, including intraoperative pain, surgical duration, postoperative recovery, and complication rates, this study provides a comprehensive assessment of intracameral lidocaine's utility.

The findings have significant clinical implications. Intracameral lidocaine emerges as a safer and more patient-friendly alternative to retrobulbar anesthesia, particularly in resource-limited settings where rapid recovery and minimal equipment requirements are paramount. Its efficacy in reducing intraoperative pain and lowering complication rates positions it as an ideal choice for high-volume cataract surgery centers. Moreover, the simplicity of administration minimizes the learning curve for practitioners, thereby enhancing its utility within primary and secondary healthcare facilities. These advantages can contribute to broader surgical accessibility and improved patient satisfaction. Further multicenter trials with diverse patient populations could provide additional insights into optimizing anesthesia strategies for cataract surgery globally.

Conclusion:

Intracameral lidocaine shows promise for cataract surgery, offering effective pain control, predictable surgery, and good visual outcomes with few complications. However, more randomized controlled trials are needed to confirm these findings and address potential confounding factors. Hospitals should consider adopting it as a standard anesthesia option, with investment in training. Future research should focus on long-term outcomes, patient satisfaction, and cost-effectiveness via multicenter trials to guide clinical practice.

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Aqueous Misdirection Syndrome in Post-trabeculectomy Patients

Rima Khan¹, Yousaf Jamal Mahsood¹

Abstract:

Objective: To determine the frequency of aqueous misdirection syndrome and its association with gender and age in post-trabeculectomy patients.

Methods: An observational study was conducted at the Department of Ophthalmology of Hayatabad Medical Complex, Peshawar, from November 2021 to May 2022. The patients who underwent uncomplicated trabeculectomy in the last two months at our department were included in this study. The data were collected for age, gender, best corrected visual acuity, time since surgery, intraocular pressures and presence or absence of aqueous misdirection syndrome. Aqueous misdirection syndrome was diagnosed if there was a shallow anterior chamber with high intraocular pressure in the presence of a patent iridectomy. Association of this complication with age and gender was also determined.

Results: A total 179 participants were recruited with a mean age of 44.30 ± 15.71 years and 103 (57.54%) male participants during the study period. The frequency of aqueous misdirection syndrome was found to be 5 (2.8%) in this study. No statistically significant association was found between development of the complication and age ($p=0.36$) and gender ($p=0.30$) of participants.

Conclusion: Aqueous misdirection syndrome is a rare complication in uncomplicated trabeculectomy surgery. Age and gender have no effect on the occurrence of aqueous misdirection in these patients. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 89-96. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Globally, glaucoma is the most common cause of irreversible vision loss ¹. It is an optic neuropathy portrayed by degradation of retinal ganglion cells with associated changes in the optic nerve head and corresponding defects in the visual field of the patient ². Raised intraocular pressure (IOP) is a crucial modifiable risk factor that accelerates ganglion cell death. Present guidelines aim to reduce intraocular pressure via pharmacological or surgical means ³. Trabeculectomy provides substantial intraocular pressure reduction and therefore remains the gold standard in glaucoma management ⁴.

Various devastating complications can occur after trabeculectomy. Malignant glaucoma, presently known under the name of aqueous misdirection syndrome (AMS), is a rare cause of secondary angle closure glaucoma ⁵. It can occur as a complication after any intraocular surgery in both open-

angle and narrow-angle patients. Von Graefe, in 1869, described this condition as being characterised by a shallow anterior chamber with raised intraocular pressure in the presence of a patent iridotomy⁶. The same study also reported an AMS prevalence of 0.37% after non-filtering surgery and 2.27% after filtering surgery in angle closure glaucoma patients. The pathogenesis is not well understood but involves anterior rotation of the ciliary body, leading to backwards flow of aqueous humour towards the vitreous, leading to increased vitreous pressure⁷. The incidence of this serious complication has been studied in various populations. According to a study conducted at Al-Shifa Trust Eye Hospital, Rawalpindi, about 1.9% of patients developed this condition after trabeculectomy⁸. However, another study reported that about 3% of their patients developed aqueous misdirection syndrome after trabeculectomy⁹.

Early identification and treatment of this condition are essential to prevent further damage to the eye, such as corneal endothelial decompensation, cataract formation, and further glaucomatous damage to the optic nerve¹⁰. The rationale for our study is that, owing to the rarity of the condition and different reports about the magnitude of this problem, we can't infer from those results. Furthermore, it is a dreadful complication, and timely intervention can save the patients' vision. That is why this study was designed to find the magnitude of this complication in our setup. This will enable us to devise treatment strategies and prevent future damage to vision in these patients.

Methodology:

An observational study was conducted in the ophthalmology department, Hayatabad Medical Complex, Peshawar, from 16th November 2021 to 16th May 2022 after ethical approval from the hospital's ethical committee. The study followed the principles of the Declaration of Helsinki. Participants aged 18-70 years who had

trabeculectomy done within the past 2 months were selected via a consecutive nonprobability sampling technique after taking a detailed informed consent. The indications of trabeculectomy included advanced glaucoma with pressures exceeding target values, progressive glaucomatous changes, uncontrolled IOP despite maximum tolerated medical therapy, and poor compliance with medication. All the trabeculectomy surgeries were performed by a single glaucoma specialist who had specialized training in glaucoma after a fellowship. The technique used in all surgeries was the same. All surgeries performed were fornix-based under local peri-bulbar anaesthesia. A corneal traction suture with 7/0 Vicryl was used to expose the superior surface of the conjunctiva. A 4 mm conjunctival flap measured with callipers was made with Westcott scissors, and wet-field cautery was used to clear the scleral vessels. and 0.4mg/ml Mitomycin-C-soaked cotton sponges were placed on the sclera for 2 min, which was then thoroughly washed with balanced saline solution. A 3x3 mm partial-thickness triangular scleral flap was made, and the trabeculectomy was performed using Kelly's punch, and the iridectomy was performed with scissors. The flap was secured with 3 slip knots using 10/0 nylon thread. A side port was made to check the patency of the bleb, and the anterior chamber was maintained. The conjunctiva was sutured with two 10/0 nylon wing sutures. Subconjunctival dexamethasone 4mg/ml was injected in the inferior fornix at the end of the surgery. Post-operatively, all patients were prescribed topical moxifloxacin eye drops four times a day, topical dexamethasone eye drops two hourly, and topical tobramycin and dexamethasone eye ointment thrice daily. Patients having previous ocular surgeries involving conjunctival manipulation, such as squint or retinal detachment surgeries, were excluded. In addition, patients who had complicated trabeculectomies were also excluded. The uncomplicated

trabeculectomy included trabeculectomy without any complications such as choroidal effusion, suprachoroidal haemorrhage, bleb leaks, or over filtration, as these can also result in shallow AC and confound results. At presentation the following clinical data were extracted from patients: Visual acuity, anterior segment examination using slit lamp biomicroscopy, intraocular pressure (IOP) measurement via Goldman tonometer and fundus examination using a 78D condensing lens. Peripheral anterior chamber depth was measured by the Van Herick method. All the data were recorded on a pre-designed proforma. Aqueous misdirection was diagnosed in post op patients if there was a shallow anterior chamber with high intraocular pressure in the presence of a patent iridectomy. Data were analysed using SPSS version 24. Continuous variables like age, time since surgery, IOP, and VA were analysed for

mean and standard deviation. For the presence or absence of aqueous misdirection syndrome (AMS), frequency and percentages were calculated. The chi-square test was applied to establish an association between the occurrence of AMS with age groups and gender of the participants. A p-value of less than 0.05 was considered significant.

Results:

The total participants recruited during the study period was 179. The mean age of the participants was 44.30 ± 15.71 years, and 103 (57.54%) were males. The baseline profile of the study group is depicted in Table 1. Out of the total, only 5 (2.8%) participants developed AMS in our study. Table 2 shows the association of the AMS with age and gender, but there was no statistically significant association.

Table 1: Demographic profile of study participants.

Characteristics (N=179)	N (%)	Mean \pm SD
Gender, n (%)	Male, 103 (57.54) Female, 76 (42.46)	
AMS, n (%)	5 (2.8)	
Mean Age (years)		44.30 ± 15.71
Mean Time since surgery (in months)		1.95 ± 0.71
Mean IOP (in mmHg)		24.06 ± 3.91
Mean Visual acuity (in LogMAR units)		1.09 ± 0.11

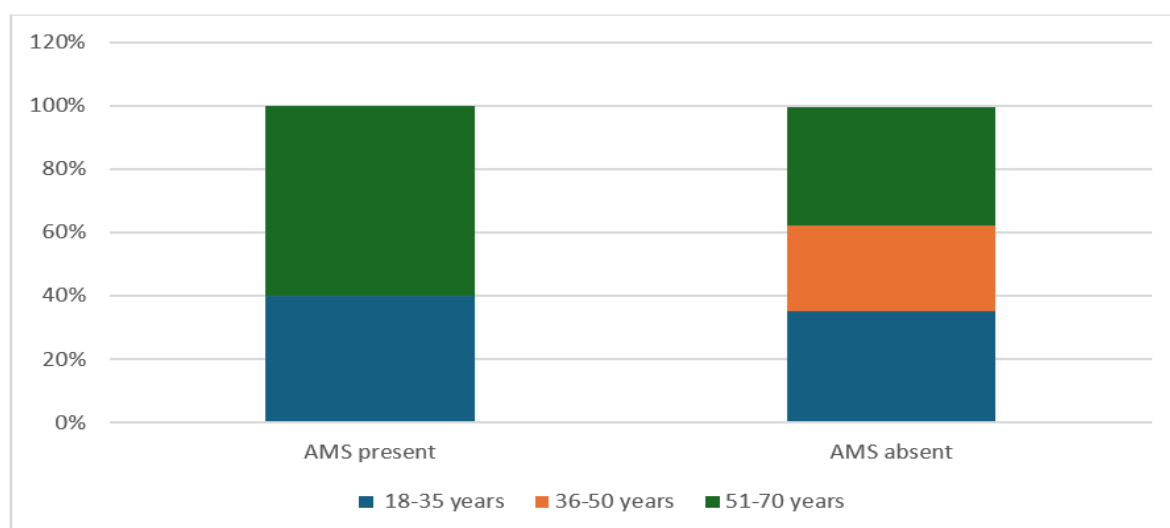


Figure 1: Distribution on aqueous misdirection syndrome (AMS) in our study participants.

Table 2: Association of aqueous misdirection syndrome with age and gender.

Characteristics (N=179)	Age distribution in years, n (%)			P- value*	Gender, n (%)		P- value*
	18 to 35	36 to 50	51 to 70		Male	Female	
AMS present	2 (40)	0 (0)	3 (60)	0.36	4 (80)	1 (20)	0.30
AMS absent	61 (35.1)	47 (27.01)	66 (37.93)		99 (56.9)	75 (43.1)	
Total, n (%)	63 (35.2)	47 (26.25)	69 (38.55)		103 (57.54)	76 (42.46)	

Discussion:

Aqueous misdirection (AMS) is a rare and challenging form of secondary angle closure glaucoma that can occur in the post-operative setting. In this cross-sectional hospital-based study, we described the frequency of Aqueous misdirection syndrome among post-trabeculectomy patients and its association with age and gender. The overall frequency of this complication was found to be 2.8% amongst our patients. This is similar to a study that reported a 3% incidence of this condition after trabeculectomy⁹. Von Graefe in 1869 reported an incidence of this complication to be 2% among post-operative glaucoma patients⁶. Similarly, a study conducted in Al-Shifa Hospital,

Rawalpindi, reported that about 1.9% of their patients developed AMS after trabeculectomy surgery⁸. Likewise, another study reported an incidence of approximately 0.6 to 4%¹¹. Our results are comparable to previous studies with a low frequency of AMS in these patients.

In our study, there was no statistically significant difference between the occurrence of this disease in males and females. This, however, is in contrast to the previous literature which claims that the condition is more common in females¹². At par with this, another study reported that the disease is more common in females with a female-to-male ratio of 7:3. According to them, the explanation for this is the more anterior position of the lens and shallower anterior chambers in the female

population¹². Annes Ahmeidat and Caroline Cobb described 3 case reports of aqueous misdirection syndrome, all occurring in Caucasian females, reiterating the increased incidence of this disease in this gender group¹³. Akin to this a case series of 66 eyes with a diagnosis of malignant glaucoma using data from the Glaucoma Division of the Stein Eye Institute, Los Angeles, from 1997 to 2022 proved that female gender was a predisposing factor for the development of this disease¹⁴. However, isolated case reports of the disease occurring in males have also been reported. Qian Qian Xu et. al reported a rare case of Aqueous misdirection syndrome occurring in a 76-year-old male patient 4 days after trabeculectomy¹⁵. This patient also later developed a ciliary detachment. Also, another case report noted in Taiwan described a 63-year-old male who developed refractory malignant glaucoma two weeks after trabeculectomy in a vasectomized eye¹⁶. On the contrary, our study showed no significant association between gender and the development of this complication. Potential reasons for the lack of gender association in our study included poor follow-up amongst female postoperative patients. Since we live in a primarily male-dominated society with low female literacy rates, females exhibited poor follow-up trends. A good proportion of female patients who visit our tertiary care hospital also come from far-flung areas and depend on menfolk for their commute. Also, there are financial constraints involved in travel to tertiary care centres. These have proved to be hindrances in their admission to our OPD, and hence, poor follow-up and lack of inclusion in our study. Also, there could be unexplored genetic predispositions amongst Pakistani men that could predispose them to the development of AMS. Further studies are needed to unveil such genetic features. The lower female participation in this study has important implications and may have influenced the results. The findings might

underestimate the experience of the female population with the condition or the results of treatment due to the small representation of women. Given possible gender-based variations in ocular anatomy, such as axial length or anterior segment features, which could affect the onset or course of aqueous misdirection syndrome, this is especially pertinent. Furthermore, hormonal variables, like postmenopausal changes, may influence trabeculectomy results or aqueous dynamics; their underrepresentation may result in an inadequate comprehension of these mechanisms. Bias in baseline characteristics may also be introduced by the skewed gender ratio. Men might show up with distinct risk profiles or disease severities, which could skew the results and cause conclusions that are disproportionately impacted by patterns unique to men. Sociocultural elements may also affect results and go unrecognised, such as disparities in access to healthcare, readiness to have surgery, or compliance with follow-up care.

Age is also considered to be an important factor in the development of this complication. A study done in Chinese patients reported an incidence of AMS to be higher among patients < 40 years of age⁶. They identified younger age as a risk factor for the development of aqueous misdirection syndrome after filtering surgery. Likewise, Zhang et al. also reported a higher prevalence of AMS among younger patients compared to older ones⁶. Similarly, another study also showed an incidence of post-operative malignant glaucoma to be about 24.1% in younger patients, which was much higher than the older patients¹⁷. They claimed that shorter axial length and more anteriorly rotated ciliary bodies may be key contributing factors for the development of malignant glaucoma in young patients with PACG after trabeculectomy. This is, in contrast with our results, which showed no statistically significant correlation between the age of patients and the development of this devastating complication. The reasons

may be different among preoperative ocular features, such as axial length, anterior chamber depth, or lens status, or genetic differences in study populations could affect susceptibility to AMS. The other possible explanation may be postoperative management protocols, differences in the aggressiveness of intraocular pressure management, use of cycloplegics, or early detection of anterior chamber shallowing may alter outcomes between studies.

Aqueous misdirection is a rare complication, most reported after trabeculectomy. Several treatment options are available⁵. Due to its rarity, however, rates of treatment success and prognosis in affected eyes are difficult to ascertain¹⁸. The difference between our results and previous literature shows the varied nature of the disease. Our study aimed to determine the frequency of this dreadful complication in our population and ensure early identification and treatment. This will prove vital in saving patients' vision. Delayed presentation has been associated with a greater chance of failure to resolve¹⁹. As a rare and intractable disease, large-scale studies on the disease are lacking. To the best of our knowledge, no such study has been conducted in our region. This study broadens our understanding of the disease in our population and alerts clinicians about its chance of occurrence, and to maintain a high index of suspicion in post op patients with high IOP and shallow anterior chambers.

Our study focuses on the importance of postoperative IOP monitoring for surgeons who have a key interest in trabeculectomy surgery. IOP measurements and looking for signs of AMS in post op patients, even months after surgery, is vital to prevent the development of this complication and enable early recognition and prompt treatment. Therefore, surgeons should formulate accurate early and late follow-up regimens for their post-trabeculectomy patients for better patient care. Nonetheless, our study also has certain limitations. A short follow-up period of only 2 months

was considered, whereas this disease can also occur many months and years postoperatively²⁰. In addition, our study was only done on Pakistani patients, and as a result, these results cannot be extrapolated to other ethnicities. Furthermore, our data lacked crucial objective parameters like refraction and axial length, which are key risk factors involved in the occurrence of this complication. The addition of these would have added more value to our results. We advise further work on the disease, keeping in mind these constraints in our study. It is advised that further work be done on this sight-threatening disease involving multicentric data with larger sample sizes.

Conclusion:

Aqueous misdirection syndrome is a rare complication in uncomplicated trabeculectomy surgery. Age and gender have no effect on the occurrence of aqueous misdirection in these patients. This study expands our knowledge of the disease in our population, cautioning clinicians about its potential occurrence and grave nature. In addition, it emphasizes the need for heightened vigilance in post op patients with elevated intraocular pressure and shallow anterior chamber.

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Histological/pathological Evaluation of Post Photo-Refractive-Keratectomy(PRK) Induced Changes in Corneal Epithelial Thickness and its Impact on Physiological Eye Functions

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Abstract:

Objectives: To evaluate histological changes and epithelial thickness (ET) post-photo refractive keratectomy (PRK) at two regions: apex of cornea (ETapex) and middle of cornea (ETmiddle). To evaluate changes of Lower Order Aberrations (LOAs), Higher Order Aberrations (HOAs), Contrast Sensitivity (CS) and Corrected Distance Visual Acuity (CDVA), and the relationship of these parameters with change of ET(apex and middle) after PRK.

Methods: Thirty-five patients, aged between 24 and 40, who had PRK were selected. Patient received eye examination, including cycloplegic refraction, non-contact intraocular pressure monitoring, slit-lamp biomicroscopy, corrected distance visual acuity (CDVA), and uncorrected visual acuity measurement. Using epithelial map of optical coherence tomography, changes in Epithelia thickness (ET) apex and ET middle were measured. Statistical Package for Social Sciences SPSS version 24 was used for data analysis.

Results: Following PRK, there was statistically significant difference in ET apex and ET middle measurements before and after surgery. ET (apex) increased after PRK, this appeared to be related to increased LOAs and increased HOAs, it was also associated with increase in CS and CDVAD (Shapiro Wilks test) with a P value of 0.006 and 0.001 respectively).

Conclusion: our study concludes that following PRK, there is a correlation between ET(apex & middle) changes and variations in CDVA, LOAs and HOAs, and SC. Post-PRK care should be tailored based involve follow-up appointments, medication, activity restrictions, sun protection, and careful monitoring of vision and healing to ensure optimal recovery and prevent complications. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 97-107. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Since its introduction in the early 1980s, photorefractive keratectomy has become a major modality in refractive surgery, particularly for low myopia. Small degrees of myopia can be effectively corrected with it, whether astigmatism is present or not. To improve vision clarity through PRK, a computer-controlled laser system called an

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Excimer Laser is used to reshape the cornea's surface so that objects focus on the retina¹. The patient lies down during this brief, painless procedure, which uses local anesthetic eye drops. An eyelid speculum is used to keep the patient's eyelids open. The computer is used to enter the degree of refractive error (such as myopia or hyperopia), and a special program is used to calculate the degree of correction². The epithelium is mechanically removed using this method of scraping. Then, to accomplish the proper change in curvature, laser is applied to both the stroma and Bowman's layer. After then, a therapeutic contact lens is applied to the cornea, and it takes three to five days for the epithelium to heal³. Its main drawbacks are post-operative pain and a delayed recovery of vision. Post-operative corneal haze is the principal complication of PRK. The natural healing process of wounds leads to corneal opacity. It first manifests 4-6 weeks after surgery and then progressively goes away over the following 3-6 months and sometimes 1-2 years⁴. The altered keratocytes change into myofibroblasts, which generate scar tissue by forming collagen. Scar tissue's ability to scatter light makes post-PRK opacification visible, and it seems to get worse as resection depth rises⁵. Research has been done on epithelial alterations and how they affect corneal refractive surgery outcomes⁶. Previous studies have demonstrated that following PRK, there is an increase in corneal thickness that happens immediately after the procedure and is observed during postoperative visits. This increase may be related to the potential regression of the refractive action that primarily occurs after PRK⁷. There are Other alternative refractive surgeries like; LASIK (Laser-Assisted in Situ Keratomileusis), that involves creating a flap in the cornea, then reshaping the underlying corneal tissue with a laser to correct refractive errors, LASEK (Laser-Assisted Subepithelial Keratectomy), Similar to PRK but involves creating a thin epithelial flap, SMILE

(Small Incision Lenticule Extraction), A minimally invasive procedure where a small incision is made, and a lenticule (thin disc-shaped tissue) is removed to correct myopia and astigmatism, ICL (Implantable Collamer Lens), a surgical procedure in which a synthetic lens is implanted inside the eye, typically used for high refractive errors or patients who are not candidates for laser surgery and Refractive Lens Exchange (RLE), a procedure where the natural lens is replaced with an artificial intraocular lens (IOL) to correct refractive errors, typically for patients with presbyopia or high refractive errors and Conductive Keratoplasty (CK), which uses radiofrequency energy to reshape the cornea, typically used for treating hyperopia (farsightedness) in older patients⁸. Still, PRK is a well-established procedure with a high rate of success; the long-term implications of epithelial changes can be significant in some cases. Epithelial irregularities, corneal scarring, dry eye syndrome, and other complications can affect vision quality and eye health. PRK can lead to long-term epithelial changes like corneal scarring, thinning, or irregularities, affecting vision. Potential issues include haze, dry eye, delayed healing, and glare. In some cases, there's a risk of regression or infections. It's important for patients considering PRK to have a thorough consultation with their eye surgeon and be aware of the potential risks and long-term effects. Regular follow-ups after surgery can help identify any problems early and allow for appropriate management⁹.

Assessment of correlations between epithelial thickness changes and key visual parameters can help to identify any significant predictors of improved or impaired visual outcomes following PRK. Very limited work is done to assess changes in corneal epithelial thickness pre- and post-Photorefractive Keratectomy (PRK) in relation to changes in vision outcomes, and a study gap exists. This study will help to identify any significant predictors of

improved or impaired visual outcomes following PRK.

Methodology:

This is a multi-centre observational study performed from April 2021 to August 2022 at (RYK Hospital-Rahim Yar Khan, Sheikh Zayed Hospital-Rahim Yar Khan, Hashmani Eye Trust Karachi). The study protocol was approved by the Sheikh Zayed Hospital (Rahim Yar Khan) ethical committee with letter no SZMCH/Ethics/2021-03/10654. Every patient provided signed informed consent. Each patient's single eye—the right eye, “oculus dexter” (OD), specifically—was assessed in this study. Participants who were pregnant or who had systemic diseases were not included in the study. Thirty-five patients, with a mean age of 28 years (range 24-40), were operated on using the PRK procedure (13 women and 22 men). The patients' refractions were stable for at least two years. Every patient had preoperative and postoperative examinations, including cycloplegic refraction, non-contact intraocular pressure monitoring, slit-lamp bio-microscopy, corrected distance visual acuity (CDVA), and uncorrected visual acuity measurement. Using the epithelial map of optical coherence tomography (Avanti XR OCT, Optovue) changes in ET apex and ET middle were measured. To use the OCT epithelial map, we examined the color-coded zones (central, mid-peripheral, peripheral) to assess thickness variations, focused on central thickness changes, and compared pre- and post-PRK for structural stability. Checked for asymmetries to identify localized healing and quantify thickness in each zone to understand remodeling patterns, and also correlated these changes with visual outcomes, like CDVA and contrast sensitivity, to assess impact on vision. Maps were tracked over time for healing progression and to identify any abnormal thinning or thickening to manage potential complications early, linking structural changes to visual quality

post-PRK. To standardize the OCT Measurements, the OCT devices were calibrated according to the manufacturer's specifications to ensure measurement accuracy. To calibrate an OCT device, it was ensured is clean and properly set up. Ran a system self-test and adjusted the focuses and signal strengths. To verify accuracy, a calibration phantom was used. Axial length and scan depth were checked, as well as image quality for clarity and repeatability.

Patients were positioned with aligned visual axes, and the same device settings were applied across pre- and post-PRK measurements to maintain consistency. Each measurement was taken multiple times, with the median value used to reduce variability and enhance reliability. Measurements were standardized at consistent pre- and postoperative intervals to monitor progressive changes. Criteria for assessment included Epithelial Thickness Measurements (middle & regional Comparison), Symmetry and Regularity, Uniformity to ensure thickness changes are uniform across zones, comparison with Baseline (pre-PRK). Clinical Impact on Visual Parameters: Correlation with Visual Acuity (CDVA) and Contrast Sensitivity.

Every patient underwent three measurements, with the mean value being utilized. Corneal Zernike coefficients (z00D-z44D) were measured with Pentacam HR (Oculus GmbH, Wetzlar, Oculus, Germany). The Freiburg Vision Test was used to determine CS, which is defined as the mean of luminance gain between a small object and its background divided by the mean background luminance (SC Weber) and its logarithm (SC Logs), both preoperatively and postoperatively¹⁰. A popular visual test battery known as "FrACT" was implied to measure contrast sensitivity, Vernier acuity, objectivity and reliability in the form of a free computer program¹¹. Measures that showed satisfactory test quality parameters were the only ones chosen. Every examination was carried out by the same technician in

complete darkness. Both before and after surgery, tests were conducted. A follow-up was performed at a fix interval of almost 1 year. To analyze the bias among observers “kappa value” was calculated and kappa value of 0.70 for present study omitted the probability of bias among observers (A **kappa value of ≥ 0.61** denotes substantial or higher agreement)

The parameters' normal distribution was evaluated using the Shapiro-Wilk test. Every continuous variable was distributed non-normally and was given as a median (range). Frequencies or percentages are used to display categorical variables. The relationships between continuous variables were assessed using Spearman's correlation coefficient. A two-tailed p-value of less than 0.05 was deemed to signify a statistically significant difference. We used IBM SPSS Statistics version 24.0 (IBM) for statistical analysis. This study focuses on how the corneal epithelium responds following PRK in relation to the parameters CDVA, CS, HOAs, and LOAs.

Results:

Out of 35 patients who underwent the PRK procedure, 13 were females and 22 were males. Their median age was 28 (range: 24–40). The preoperative and 12-month postoperative (PRK) characteristics related to visual acuity, contrast sensitivity, and

corneal epithelial thickness in the right eye (OD) of participants, based on median values and ranges (with 95% confidence interval) demonstrated that Pre-operative CDVA (logMAR) had median value of -0.160, with values ranging from -0.160 to 0.070 and 12 Months Postoperative CDVA slight decreased in median acuity (-0.130), with a broader range from -0.160 to 0.290. (See Table-1)

Data highlights the diverse postoperative changes in visual and structural parameters of the cornea, with a trend toward stability in epithelial thickness and some improvement in contrast sensitivity, while changes in corneal aberrations appear minimal but individualized. (Refer to Table-2)

Data in table-3 (with 95% confidence interval) demonstrated variable outcomes, some variables showed significant positive correlation and a few showed significantly negative correlations.

We also observed a statistically significant negative correlations between the median value of CDVAD (logMar) and the median value of SCD (weber) (Spearman's rho:-0.407, p=0.035), (See Table 3)

The key findings of the study and their possible implications have been organized into positive and negative correlations, highlighting the statistical relationships and their clinical implications. (See Table 4)

Table-1: Visual characteristics of participants and demographics.

Variable	Median	Minimum	Maximum
Age (years)	28	24	40
CDVA (logMar) preop	-0.160	-0.160	0.070
CDVA(logMar)12months	-0.130	-0.160	0.290
SC (weber) preop	0.000	-1.780	2.110
SC (weber) 12 months	0.380	0.220	2.360
CS (logcs) preop	2.290	1.630	7.770
CS (logcs) 12 months	2.330	1.630	2.650
ETmiddle (μm) preop	54	46	68
ETmiddle (μm) 12months	53	47	68
ETapex (μm) preop	54	45	68
ET apex (μm) 12 months	54	48	68
z00 (D) preop	134.93	111.216	161.105
z00D 12 months	133.06	111.216	161.105

z11D preop	1.528	0.494	5.893
z11D 12 months	1.368	0.214	5.893
z02D preop	79.037	66.655	95.948
z02D 12 months	78.951	66.655	95.948
z22D preop	1.013	0.378	2.440
z22D 12 months	0.821	0.222	1.684
z31D preop	0.319	0.054	0.823
z31D 12 months	0.333	0.081	0.823
z33D preop	0.193	0.039	1.285
z33D 12 months	0.215	0.067	1.285
z40D preop	1.743	0.847	2.757
z40D 12 months	1.487	0.847	2.757
z42D preop	0.117	0.019	3.510
z42D 12 months	0.159	0.021	0.302
z44D preop	0.100	0.029	0.437
z44D 12 months	0.108	0.021	0.437
Gender	N	%	
Females	13	37.14	
Males	22	62.85	
*OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: Epithelial thickness changes(corneal apex); ET middle: Epithelial Thickness (middle of the cornea); preop: preoperative.			

Table-2: Values of variance (preoperative value - postoperative 12 months value & Zernike coefficients)

Variable	Median	Minimum	Maximum
CDVAD (log Mar)	0.000	-0.230	0.450
SCD (weber)	0.550	0.220	2.360
CSD (logcs)	0.000	-6.000	0.890
ETmiddle (μm)	0.000	-18.00	18.00
ETapex (μm)	0.000	-18.00	17.00
z00D	-0.090	-40.49	29.97
z11D	-0.160	-24.84	17.29
z22D	-0.224	-1.490	1.270
z31D	0.039	-0.510	0.510
z33D	-0.010	-1.160	1.050
z40D	-0.297	-1.610	1.670
z42D	0.025	-0.140	0.280
z44D	-0.014	-0.360	0.350
OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: Epithelial Thickness changes at the corneal apex; ET middle: Epithelial Thickness changes at the middle of the cornea.			

Table 3: Correlation between the median values of variance of different variables for OD.

Variable (OD)		CD VA D log Mar	SC D weber	CS D log cs	ET Mid dle (μ m)	ET ape x (μ m)	Zernike polynomials (optical aberration types)								
							z00 D	z11 D	z02 D	z22 D	z31 D	z33 D	z40 D	z42 D	z44 D
CDVAD logMar	S.man's rho	1.000	-0.407	-0.354	-0.404	-0.419	0.647	-0.317	0.626	0.262	-0.096	0.012	-0.645	-0.278	0.362
	P	.	0.035*	0.070	0.037*	0.030*	0.001*	0.107	0.001*	0.187	0.634	0.953	0.001*	0.161	0.063
SCD (weber)	S.man's rho	-0.407	1.000	0.410	0.488	0.354	-0.252	0.009	-0.221	-0.210	0.191	-0.274	0.295	0.298	-0.316
	P	0.035*	.	0.034	0.010*	0.070	0.205	0.966	0.267	0.294	0.340	0.167	0.135	0.131	0.109
CSD (logcs)	S.man's rho	-0.354	0.410	1.000	0.325	0.323	-0.185	0.013	-0.144	-0.346	0.031	-0.516	0.247	-0.050	-0.329
	P	0.070	0.034*	.	0.098	0.101	0.355	0.951	0.472	0.077	0.877	0.006*	0.214	0.805	0.094
ETmiddleD (μ m)	S.man's rho	-0.404	0.488	0.325	1.000	0.885	-0.512	0.319	-0.479	-0.336	0.402	-0.048	0.612	0.454	-0.214
	P	0.037*	0.010*	0.098	.	0.001*	0.006*	0.105	0.011*	0.086	0.038*	0.814	0.001*	0.017*	0.284
ETapexD (μ m)	S.man's rho	-0.419	0.354	0.323	0.885	1.000	-0.562	0.405	-0.521	-0.326	0.501	-0.155	0.652	0.417	-0.323
	P	0.030*	0.070	0.101	0.001*	.	0.002*	0.036*	0.005*	0.097	0.008*	0.441	0.001*	0.030*	0.101
z00D	S.man's rho	0.647	-0.252	-0.185	-0.512	-0.562	1.000	-0.337	0.982	0.435	-0.241	0.103	-0.565	-0.281	0.225
	P	0.001*	0.205	0.355	0.006*	0.002*	.	0.086	0.001*	0.023*	0.226	0.609	0.002*	0.156	0.259
z11D	S.man's rho	-0.317	0.009	0.013	0.319	0.405	-0.337	1.000	-0.314	0.081	0.659	0.256	0.721	0.359	0.256
	P	0.107	0.966	0.951	0.105	0.036*	0.086	.	0.111	0.689	0.001*	0.197	0.001*	0.066	0.198
z02D	S.man's rho	0.626	-0.221	-0.144	-0.479	-0.521	0.982	-0.314	1.000	0.413	-0.228	0.050	-0.527	-0.250	0.248
	P	0.001*	0.267	0.472	0.011*	0.005*	0.001*	0.111	.	0.032*	0.252	0.804	0.005*	0.208	0.211
z22D	S.man's rho	0.262	-0.210	-0.346	-0.336	-0.326	0.435	0.081	0.413	1.000	0.144	0.263	-0.208	-0.107	0.455
	P	0.187	0.294	0.077	0.086	0.097	0.023*	0.689	0.032*	.	0.473	0.185	0.299	0.597	0.017*
z31D	S.man's rho	-0.096	0.191	0.031	0.402	0.501	-0.241	0.659	-0.228	0.144	1.000	0.021	0.387	0.328	-0.029

	P	0.63 4	0.3 40	0.8 77	0.0 38*	0.0 08*	0.2 26	0.0 01*	0.2 52	0.4 73	.	0.9 16	0.0 46*	0.0 95	0.8 87
z33D	S.m an's rho	0.01 2	- 0.2 74	- 0.5 16	- 0.0 48	- 0.1 55	0.1 03	0.2 56	0.0 50	0.2 63	- 0.0 21	1.0 00	0.2 43	- 0.0 88	0.3 25
	P	0.95 3	0.1 67	0.0 06*	0.8 14	0.4 41	0.6 09	0.1 97	0.8 04	0.1 85	0.9 16	.	0.2 22	0.6 64	0.0 98
z40D	S.m an's rho	- 0.64 5	0.2 95	0.2 47	0.6 12	0.6 52	- 0.5 65	0.7 21	- 0.5 27	0.2 08	0.3 28	0.2 43	1.0 00	0.3 69	0.0 23
	P	0.00 1*	0.1 35	0.2 14	0.0 01*	0.0 01*	0.0 02*	0.0 01*	0.0 05*	0.2 99	0.0 95	0.2 22	.	0.0 58	0.9 09
z42D	S.m an's rho	- 0.27 8	0.2 98	- 0.0 50	0.4 54	0.4 17	- 0.2 81	0.3 59	- 0.2 50	- 0.1 07	0.3 87	- 0.0 88	0.3 69	1.0 00	0.0 42
	P	0.16 1	0.1 31	0.8 05	0.0 17*	0.0 30*	0.1 56	0.0 66	0.2 08	0.5 97	0.0 46*	0.6 64	0.0 58	.	0.8 37
z44D	S.m an's rho	0.36 2	- 0.3 16	- 0.3 29	- 0.2 14	- 0.3 23	0.2 25	0.2 56	0.2 48	0.4 55	- 0.0 29	0.3 25	0.0 23	0.0 42	1.0 00
	P	0.06 3	0.1 09	0.0 94	0.2 84	0.1 01	0.2 59	0.1 95	0.2 11	0.0 17*	0.8 87	0.0 98	0.9 09	0.8 37	.
*OD: right eye; CDVA: Corrected Distance Vision Acuity; SC: Sensitivity Contrast; CS: Contrast Sensitivity; logcs: log of CS; ET apex: epithelial thickness changes at the corneal apex; ET middle: epithelial thickness changes at the middle of the cornea; S.man's rho: Spearman's rho.															

Table 4: Key findings along with p value and implications

Correlation	P value	Key observation/implications
Positive correlations		
CDVAD (L-M) ↔ z00D	0.001	Changes in corneal structure negatively impact vision
CDVAD (L-M) ↔ z02D	0.001	Increased ghosting, halos, or starbursts
SCD (W) ↔ CSD (LCS)	0.034	Improved outcomes in low-light conditions
SCD (W) ↔ ET middle	0.010	Indicates corneal structural consistency post-surgery
ET middle ↔ ET apex	0.001	Balanced corneal healing across the cornea.
ET middle ↔ z31D	0.038	Positive association with specific aberrations
ET middle ↔ z40D	0.001	increase in epithelial thickness linked to spherical aberration
ET middle ↔ z42D	0.017	Indicates correlation with higher-order aberrations
ET apex ↔ z11D	0.036	Associated with coma-related aberrations
ET apex ↔ z31D	0.008	Corneal apex thickness linked to coma type aberration
ET apex ↔ z40D	0.001	Indicates development of spherical aberrations
ET apex ↔ z42D	0.030	Positive association with higher-order aberrations
z00D ↔ z02D	0.001	Significant correlation between two aberrations
z00D ↔ z22D	0.023	Defocus & astigmatic aberrations correlate
z11D ↔ z31D	0.001	Changes in coma-related aberrations
z11D ↔ z40D	0.001	Predicts impact on visual acuity & clarity in low light
z02D ↔ z22D	0.032	Suggests compounding effects of multiple aberrations
z22D ↔ z44D	0.017	Indicates interconnected visual distortions

z31D ↔ z40D	0.046	Increases in one aberration linked to others
Negative correlations		
CDVAD (L-M) ↔ SCD (W)	0.035	Increased contrast sensitivity linked to improved visual acuity.
CDVAD (L-M) ↔ ET apex	0.030	Increased corneal apex stability linked to better visual acuity.
CDVAD (L-M) ↔ ET middle	0.037	Stable epithelial thickness linked to increased visual clarity.
CDVAD (L-M) ↔ z40D	0.001	↓ spherical aberrations associated with ↑ visual acuity
CSD (LCS) ↔ z33D	0.006	↑ contrast sensitivity co-related with ↓ coma aberration
ET middle ↔ z00D	0.006	↓ aberrations associated with ↑ epithelial stability.
ET middle ↔ z02D	0.011	↓ aberrations linked to stable epithelial thickness.
ET apex ↔ z00D	0.002	Improved corneal apex linked to fewer aberrations.
ET apex ↔ z02D	0.005	Stable corneal apex thickness linked to ↓ visual deforms
z00D ↔ z40D	0.002	↓ defocus correlated with ↓ spherical aberration.
z02D ↔ z40D	0.005	↓ interconnected aberrations lead to improved clarity
logMar=LM, Weber=W, logCS=LCS, ET		

Discussion:

In this study, we looked into how LOAs, HOAs, CS, and CDVA after PRK were affected with the thickness of the corneal epithelium at the middle and apex. According to our research, ET increased following PRK and this was correlated with higher HOAs (Z31, Z40, and Z42) and LOAs (Z11) similar findings were reported by Mirafteb and Gialelis^{12,13} that following PRK, the treated eye's visual output decreases and ocular aberrations increase. Additionally, it appears that the decline in LOAs (Z00, Z02) and the improvement in CDVA are connected to the rise in ET apex. Furthermore, we showed that ET middle rose following PRK and that ET apex, CS, and HOAs (Z31, Z40, and Z42) all seemed to rise in tandem with and it is in agreement with Ahmed A et al¹⁴. Also, the decrease in LOAs (Z00, Z02) and the decrease in CDVA appeared to be related to the increase in ET middle and We also showed that an increase in CDVA is associated with an increase in LOAs (Z00, Z02). The

increase in CDVA was related to the decrease in CS, ET apex, ET middle and HOAs (Z40), one possible reason for it may be that after accelerated corneal cross-linking (aCXL), there is an initial increase in corneal densitometry, which subsequently decreases over time, aligning with preoperative values by approximately one year post-procedure this finding agrees with Stein et al¹⁵. Lastly, a decrease in HOAs is linked to an increase in CS (Z33) and it is plausible that this is because, in PRK, an epithelium has been removed, and the quality of the epithelial cells that regenerate differs. Changes in the quality of the newly formed epithelial cells, variations in the specific cells' clarity, and variations in the new cells' size and shape are all caused by this process of epithelial cell regeneration, Khodaparast et al¹⁶.

HOAs rise during the remodeling of the epithelium following PRK surgery. A significant increase in spherical aberration may be linked to alterations in the corneal epithelium one year following PRK¹⁷⁻²⁰. A

previous study concluded that following PRK, CS improved and HOAs rose and also stated that HOAs rose following PRK²¹. PRK induced LOAs and HOAs decreased with passing time gradually²². HOAs rose following PRK in short term and this finding is in agreement with our study²³.

After PRK, the corneal epithelium undergoes remodeling to smooth the surface and compensate for irregularities in the underlying stromal tissue. This remodeling can sometimes increase or unevenly distribute epithelial thickness and result in corneal shape alterations, which can influence higher-order aberrations (HOA), including spherical aberrations which can have an Impact on Visual Quality (blurred or distorted vision, halos, glare or reduced contrast sensitivity). In agreement with our study, Beser et al even showed that spherical aberration (Z40) increased a year after surgery, but there was no significant difference in coma and trefoil evaluation between preoperative and postoperative values following PRK²⁴. Persistent spherical aberrations due to epithelial changes may necessitate additional interventions, such as wavefront-guided enhancements or customized re-treatments, to minimize aberrations and improve visual outcomes. According to Zhang et al, PRK-induced epithelial remodeling can affect future refractive procedures by altering corneal stability, topography, and healing responses²⁵. It's important to carefully evaluate the cornea's condition before proceeding with any additional surgeries, and strategies like corneal strengthening treatments or different surgical approaches may be considered to mitigate risks.

The small sample size that was examined in this study was one of its shortcomings. Follow-up time is yet another restriction. Patients may have certain shared characteristics, such as higher health awareness and socioeconomic status, which

can lead to results that are not fully generalizable to the broader population. **Limited Control over Sample Size and Composition** does not allow for controlling key sample characteristics (age, gender, disease severity), which may result in imbalanced groups, weakening the study's ability to detect meaningful differences. Longer-term research on epithelial change and its correlation with the other parameters would be beneficial.

Conclusion:

It was demonstrated that the shift in the ET apex, which is in front of the patient, is connected to the shift in the CS. Any alteration in the ET middle results in an equivalent alteration in the CS. The study also highlights the importance of tailoring follow-up care and monitoring plans to each patient's specific needs after undergoing photorefractive keratectomy (PRK). This approach considers individual factors such as healing response, pre-existing eye conditions, lifestyle, and risk factors to optimize recovery, prevent complications and ensure the best possible visual outcomes. Personalized protocols may include customized schedules for check-ups, targeted treatments, or adjustments in medications based on the patient's progress.

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Association of Age Groups, Gender, Smoking, and Hypertension with Pan-Retinal Photocoagulation Sessions in Diabetic Retinopathy Patients in the Population of D.I. Khan

Muhammad Shoaib Khan¹, Muhammad Kamran Khalid¹, Muhammad Sharjeel¹, Muhammad Abdullah¹, Hidayatullah Mahsud²

Abstract:

Objectives: To evaluate age groups, gender, smoking, and hypertension as risk factors for requiring more than one session of pan-retinal photocoagulation (PRP) and the severity of DR in the population of D.I. Khan.

Methods: This cross-sectional study was conducted at the Eye Unit of Gomal Medical College, Dera Ismail Khan, from January to December 2023. Patients undergoing single or multiple PRP sessions during this period were included. Consecutive, non-probability sampling was used, and data were analyzed using SPSS version 23.

Results: Of the 84 patients included, 52 (61.90%) were male, and 32 (38.10%) were female. Age above 50 and hypertension were significant risk factors for requiring more than one PRP session ($p = 0.006$ and $p = 0.031$, respectively). Gender and smoking were not statistically significant risk factors.

Conclusion: Hypertension and older age are significant risk factors for multiple PRP sessions and the severity of DR in the population of D.I. Khan. Managing these modifiable risk factors may reduce the need for repeated treatments. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 108-112. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Diabetic retinopathy (DR) is one of the most prevalent ocular complications in the diabetic population worldwide ^{1,2}. It is a leading cause of preventable blindness, particularly in middle-aged and elderly individuals ³. Fortunately, vision loss due to DR is preventable, and the incidence of such loss has decreased over the past two decades ⁴. This improvement is attributed to better control of systemic risk factors, advancements in disease evaluation, screening programs, and newer management strategies, such as the widespread adoption of the Early Treatment of Diabetic Retinopathy Study (ETDRS) classification system ⁵.

Pan-retinal laser photocoagulation (PRP) is the standard treatment for proliferative DR (PDR) and advanced disease, effectively preventing sight-threatening complications ⁶. The introduction of pattern scan laser (PASCAL) technology has made PRP faster, easier to perform, and more comfortable for patients ⁷. Additionally, advancements in diagnostic tools like

optical coherence tomography (OCT) and intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapies have significantly improved the management of diabetic macular edema (DME)⁸. In current eras, there are different anti-VEGF agents available for managing different DR complications e.g. bevacizumab, ranibizumab, and aflibercept⁹. While for PDR, Scatter, or pan-retinal photocoagulation is preferred. Both management's plans have a good outcome in halting the advancement in DR¹⁰.

The D.I. Khan region has a high prevalence of diabetes and limited access to specialized ophthalmic care, making it an important area for studying DR management and risk factors. This study aims to address the lack of data on the association of age groups, gender, smoking, and hypertension with the number of PRP sessions required in DR patients in this region.

Methodology:

This descriptive cross-sectional study was conducted at the Eye Department of Gomal Medical College, D.I. Khan, from January to December 2023. Ethical approval was obtained from the institutional review board of Gomal Medical College.

All diabetic retinopathy patients undergoing PRP during the study period were included, except those with concurrent retinal diseases (e.g., retinal vein occlusion) or prior vitreoretinal surgery. Consecutive, non-probability sampling was used.

PRP was performed using a mono-spot slit-lamp delivery system (Nidek GYC-1000, Japan) under topical anaesthesia. Laser

power ranged from 200–400 mW, spot size was 200–500 μm , and duration was 0.1–0.2 seconds. All procedures were performed by experienced ophthalmologists with over 5 years of practice.

The sample size was calculated assuming a diabetic retinopathy population of 20,000, with a 30% proportion of patients requiring more than one PRP session, a 95% confidence interval, and a 9.8% margin of error, yielding a sample size of 84. A 9.8% margin of error was chosen to balance precision and feasibility, given the limited resources and patient population in the region.

Data were analysed using SPSS 23. Chi-square tests were used to compare categorical variables, and logistic regression was performed to calculate odds ratios for significant risk factors. P-values < 0.05 were considered statistically significant.

Results:

Of the 84 patients included, 52 (61.90%) were male, and 32 (38.10%) were female. The majority (67.86%) were above 50 years of age. Hypertension was present in 31 patients (36.90%), with 22 (26.19%) having controlled hypertension and 9 (10.71%) having uncontrolled hypertension.

Patients above 50 years were significantly more likely to require multiple PRP sessions ($p = 0.006$). No significant association was found between gender and the number of PRP sessions ($p = 0.732$). Smoking was not a significant risk factor for multiple PRP sessions ($p = 0.568$). Hypertension was significantly associated with multiple PRP sessions ($p = 0.031$).

Table 1: Comparison of age and gender with PRP sessions

PRP sessions	Gender		Chi-Square	P-value
	Male	Female	0.117	0.732
First session	28	16		
Multiple sessions	24	16		
	Age of patients		7.507	0.006
	age 50 or below	age 50 or below		
First session	20	24		
Multiple sessions	7	33		

Table 2: Comparison of smoking history with PRP sessions

PRP sessions	Smoking history		Chi-Square	P-value
	Yes	No	0.327	0.568
First session	2	42		
Multiple sessions	3	37		

Tab 3. Comparison of HTN status with the PRP session

PRP sessions	HTN status			Chi-Square	P-value
	Controlled HTN	Uncontrolled HTN	No HTN	6.921	0.031
First session	13	08	23		
Multiple sessions	09	01	30		

Discussion:

This study evaluated the association of age groups, gender, smoking, and hypertension with the number of pan-retinal photocoagulation (PRP) sessions required in diabetic retinopathy (DR) patients in the D.I. Khan region. Our findings indicate that age above 50 and hypertension are significant risk factors for requiring multiple PRP sessions, while gender and smoking did not show a statistically significant association.

The significant association between older age (above 50 years) and multiple PRP sessions aligns with previous studies. Satoshi Kato et al. (2002) demonstrated that the prevalence of DR increases with age, even in patients with a shorter duration of diabetes, suggesting that aging itself may exacerbate retinal vascular changes¹¹. This is further supported by the natural progression of DR, which tends to be more aggressive in older patients due to cumulative exposure to hyperglycemia and other systemic risk factors. Our findings underscore the importance of early screening and intervention in older diabetic patients to prevent the progression of DR and reduce the need for repeated laser treatments.

Hypertension emerged as a significant risk factor for multiple PRP sessions in our study, consistent with findings from Yu-Ting Li et al. (2021) and Tahir Masaud Arbab et al. (2008)^{15,16}. Hypertension exacerbates retinal vascular damage by increasing shear stress and endothelial dysfunction, leading to more severe DR and a higher likelihood of requiring additional PRP sessions. These findings highlight the need for integrated management of diabetes and hypertension to mitigate the progression of DR and reduce the burden of treatment.

Contrary to some studies, we found no significant association between gender and the need for multiple PRP sessions. For instance, Rajiv Raman et al. (2009) reported a higher prevalence of DR in males, which they attributed to differences in healthcare-seeking behaviour and systemic risk factors¹². Similarly, Sara Cherchi et al. (2020) found that DR was more prevalent in men, possibly due to hormonal and lifestyle differences¹³. The lack of association in our study may reflect regional variations in gender-related risk factors or differences in sample characteristics.

Similarly, smoking did not show a significant association with multiple PRP sessions in our study. This contrasts with findings by Xiaoling Cai et al. (2018), who reported that smoking increased the risk of DR in type 1 diabetes but decreased it in type 2 diabetes¹⁴. The discrepancy may be due to the relatively low prevalence of smoking in our study population or differences in the distribution of diabetes types. Further studies with larger sample sizes are needed to explore these associations in greater depth.

Our findings have important clinical implications for the management of DR in resource-limited settings like D.I. Khan. Early identification and management of modifiable risk factors, such as hypertension, can help reduce the need for multiple PRP sessions and improve patient outcomes. Additionally, targeted screening programs for older diabetic patients may facilitate early detection and treatment of DR, preventing vision-threatening complications.

This study provides valuable insights into the risk factors influencing PRP sessions in a region with limited access to specialized ophthalmic care. However, several limitations should be acknowledged. First, the study did not account for potential confounding factors such as duration of diabetes, HbA1c levels, or socioeconomic status, which may influence the severity of DR and the need for multiple PRP sessions. Second, the use of consecutive, non-probability sampling may introduce selection bias, limiting the generalizability of the findings. Future studies with larger, more diverse samples and longitudinal designs are needed to validate these results and explore additional risk factors.

This study found that age above 50 and hypertension are significant risk factors for requiring multiple PRP sessions, consistent with previous research^{11,15}. Gender and smoking did not show a significant association, contrasting with some studies that reported higher DR prevalence in males and smokers^{12,14}. These

discrepancies may be due to regional variations in risk factor prevalence or study design differences.

Improved blood pressure control and early intervention strategies may reduce the need for multiple PRP sessions, highlighting the importance of integrated diabetes and hypertension management. This study did not account for potential confounding factors such as duration of diabetes, HbA1c levels, or socioeconomic status, which may influence the need for multiple PRP sessions.

Conclusion:

Age above 50 and hypertension are significant risk factors for multiple PRP sessions in DR patients. Managing these factors may reduce the need for repeated treatments and improve DR outcomes.

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Disorganization of Retinal Inner Layers in Diabetic Patients

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Abstract:

Objective: To investigate the prevalence of Disorganization of Retinal Inner Layers (DRIL) in patients with diabetes and its relationship with Diabetic Macular Edema (DME) and initial visual acuity.

Methods: This cross-sectional study involved 96 patients aged between 30-70 years with diabetes who underwent spectral-domain optical coherence tomography (SD-OCT) scans to evaluate Disorganization of Retinal Inner Layers (DRIL) and Diabetic Macular Edema (DME). Data were entered and analyzed using SPSS version 23.

Results: Out of 96 patients, 46 (47.9%) were males and 50 (52.1%) were females. Diabetic Macular Edema (DME) was found in 60 (62.5%) patients. There was a significant association between the existence of diabetic macular edema and DRIL. The findings revealed that DRIL was present in 44.8% of patients and was significantly linked to central foveal thickness and visual acuity.

Conclusion: The study suggests that DRIL is a valuable indicator for predicting visual outcomes in patients with DME. The presence and extent of DRIL may also have prognostic implications, helping clinicians to identify patients who are at higher risk of vision loss. *Al-Shifa Journal of Ophthalmology* 2025; 21(2): 113-. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Diabetes mellitus is a global epidemic with profound effects on the retinal microvasculature. Diabetic macular edema is characterized by the buildup of fluid within the retina (intraretinal) and beneath the retina (subretinal), as a consequence of failure of the blood retinal barrier, leading to swelling and thickening of the macula. It is the leading cause of visual impairment in diabetic retinopathy. Diabetic macular edema (DME) is a complex condition that develops due to a combination of factors, including chronically elevated blood sugar levels, damage to the vascular endothelium, and a disrupted balance of growth factors and cytokines. Over time, chronic edema can lead to permanent structural changes, including: Disruption of the retinal layers, cystoid spaces, retinal fibrosis, and vision loss^{1, 2}.

The Early Treatment Diabetic Retinopathy Study (ETDRS) identified central retinal thickness, via slit lamp biomicroscopy and Color fundus photographs, as potential markers to guide treatment for diabetic macular edema. However, small changes in

retinal thickness cannot be assessed via these methods due to their subjective nature. The problem was partially resolved by the subsequent availability of time-domain optical coherence tomography (OCT) as it precisely quantified the overall retinal thickness, but later studies suggested that, although overall retinal thickness is related to visual acuity, it is only to a moderate extent³.

The commencement of landmark investigation in ophthalmology, spectral-domain OCT (SD-OCT), enabled the production of high-resolution images of retinal layers and hence improved the ability to detect retinal pathology in individual layers. Previous research has reliably predicted two of the SD-OCT biomarkers, the intactness of the external limiting membrane (ELM) and ellipsoid zone (EZ), to be consistently related to visual acuity in diabetic macular edema⁴.

In 2014, Sun et al were the first to identify disorganization of the retinal inner layers (DRIL) as a potential SD-OCT biomarker to be related to visual acuity, such that changing the former predicted changes in the latter. Disorganized Retinal Inner Layers (DRIL) refers to the width (in micrometers) of the area where the normally distinct boundaries between three key retinal layers - the ganglion cell layer-inner plexiform layer (GCL-IPL) complex, inner nuclear layer (INL), and outer plexiform layer (OPL) - become indistinct and cannot be identified on Spectral-Domain Optical Coherence Tomography (SD-OCT) scans. Disorganization of the retinal inner layers (DRIL) is a characteristic feature of various retinal diseases, including diabetic macular edema (DME), retinal vein occlusion, and age-related macular degeneration. The pathogenesis of DRIL involves a complex interplay of factors, including cytotoxic edema, neurodegeneration, Müller cell (the primary glial cells of the retina) dysfunction, release of pro-inflammatory cytokines, ischemia culminating in tissue hypoxia, increased permeability of retinal

vessels, and retinal layer remodeling. These factors contribute to the disorganization of the inner retinal layers, characterized by: Loss of clear layer boundaries, Cell death and migration, Axonal disruption, and Synaptic loss¹. Another observational case series demonstrated that the presence of DRIL exaggerated diabetic retinopathy⁵. In a recent study, patients who had non-proliferative diabetic retinopathy and naïve center-involved diabetic macular edema were studied for the presence of DRIL, and the frequency of DRIL turned out to be 52.63%⁶. Another cross-sectional study investigated the impact of DEX (dexamethasone) implant on DRIL in DME. They reported the frequency of DRIL at baseline to be 52.5% and regarded it as a negative prognostic factor⁷. DRIL can lead to significant visual impairment, as the inner retinal layers play a critical role in transmitting visual information from the photoreceptors to the brain. Santos et al. in their study demonstrated DRIL as a predictor of poor visual outcome after treatment with anti-VEGF (vascular endothelial growth factor) therapy for diabetic macular edema⁸. Furthermore, after diabetic macular edema subsides, the resolution pattern of DRIL predicts the visual acuity⁹. Another study revealed that every 100µm increase in DRIL corresponds to a decline of approximately 6 letters in ETDRS score⁵.

There is no study to date on the frequency of DRIL in DME and its association with BCVA in our population. Furthermore, the significance of identifying this baseline OCT biomarker in diabetic macular edema cannot be neglected, as it will help in gaining better insight into disease management. It will also provide a direction to further longitudinal studies and clinical trials in this area that may explore the response of diabetic macular edema with DRIL to conventional management options. This study aimed to enhance our understanding of retinal layer disruption (DRIL) in treatment-naïve patients, focusing on its early detection and

relationship with best-corrected visual acuity (BCVA). Furthermore, we also sought to determine if any direct association exists between the length of DRIL and central foveal thickness.

To determine the frequency of Disorganization of Retinal Inner layers (DRIL) in Diabetic patients and its association with diabetic macular edema (DME) and baseline best corrected visual acuity.

Methodology:

This study employed an observational cross-sectional design, featuring prospective enrollment of participants. The study was conducted in the Department of Ophthalmology Unit II, Dr Ruth K.M Pfau, Civil Hospital, Dow University of Health Sciences, Karachi. With the help of WHO sample size calculator, taking statistics for the frequency of DRIL as 52.63%⁶, confidence interval 95%, and margin of error as 10%, the sample size calculated was 96. After getting approval from the institute's Ethical Review Board, the study was conducted from May 2024 to October 2024. Patients presenting in the OPD were enrolled in the study after giving informed written consent. Patients aged between 30-70 years, having Type 1 or Type 2 DM, were included in study. While patients having cataract or any other significant media opacity, who had cataract or any other surgery done within past 6 months, administered Intravitreal anti-VEGF agents and Intravitreal steroid therapy, were excluded from study.

Patients were divided into four groups based on their best corrected visual acuity, as follows:

No visual loss (6/6-6/9): 42 (44.8%)

Mild visual loss (6/12-6/18): 27 (28.1%)

Moderate Visual loss (6/24-6/36): 14 (14.6%)

Severe visual loss (6/60 or less): 12 (12.5%)

Questionnaires were filled out by asking questions in the local language. Variables, including demographics, duration of presentation, and type of diabetes, were

noted on a predesigned questionnaire. A comprehensive ophthalmic evaluation was conducted on all patients, consisting of a thorough medical history and a series of diagnostic tests. Visual acuity was assessed using the Snellen chart, while intraocular pressure was measured through applanation tonometry. Confrontation visual field testing and pupillary reaction assessment were also performed to evaluate peripheral vision and neurological function. Additionally, extraocular movements were evaluated to assess eye alignment and motility. A slit lamp examination was conducted to scrutinize the anterior segment, including the cornea, iris, and lens, as well as the posterior segment, comprising the vitreous and retina. Finally, a fundus examination was performed using indirect ophthalmoscopy to provide a detailed view of the retina and its blood vessels. Spectral-domain OCT was performed on all patients enrolled in the study after taking consent and explaining the procedure. All the OCT scans of enrolled patients were performed by a single senior technician. All the scans, including 3D macula and 5-line cross report, were scrutinized for diabetic macular edema and DRIL. Central foveal thickness, within the 1mm zone centered on the fovea, in micrometers, and horizontal extent of DRIL in micrometers were also recorded for each patient. Several scans with DRIL were also recorded for each patient. Central thickness was analyzed using the classical 6*6mm 3D macula report. In addition to central thickness, it also presents macular thickness and total volume on the ETDRS grid. DRIL was assessed using 5 horizontal B-scans (two scans above and below the foveal scan line) by two retinal specialists independently. In case of any disagreement between the two, the case was discussed between them until a final consensus was reached. The horizontal extent of DRIL was measured in each scan through a software caliper, and global DRIL was calculated by taking the average measurement of all five scans.

Data were entered and analyzed using SPSS version 23. For quantitative variables, normality was assessed by Shapiro Wilk test. Mean and standard deviation/median and interquartile ranges were computed for age, central foveal thickness, and horizontal extent of DRIL. Frequency and percentages were computed for gender, the type of diabetes, therapy used, and presence and/or absence of DRIL. P-value less than or equal to 0.05 was taken as significant. The confidence interval was taken as 95%.

Results:

The study examined 96 eyes from 96 patients suffering from diabetes mellitus. Of these, 46 (47.9%) were males and 50 (52.1%) were females. 19 (19.8%) patients had Type 1 diabetes, and 77 (80.2%) patients had Type 2 diabetes. The mean age of participants was 59.2 ± 9.47 . 51 (53.1%) patients were using oral hypoglycemic for managing blood sugar levels, 19 (19.8%) were using insulin, while 26 (27.1%) were using both oral hypoglycemic and insulin.

The mean central foveal thickness of the patients in the study was 296.53 ± 123.43 . DRIL was identified in 43 (44.8%) patients (Figure 1). The mean of the horizontal extent of DRIL in these patients was $352.18 \mu\text{m} \pm 147.91$. Similarly, the presence of DRIL was not affected by gender ($p = 0.871$). The type of therapy (oral hypoglycemic, insulin and oral hypoglycemic combined with insulin) had no significant association with the occurrence of DRIL ($p = 0.130$). There was no correlation between the age of the patient and horizontal extent of DRIL in micrometers ($p = 0.351$). However, it was found that type 1 diabetics had statistically lower horizontal extent of DRIL ($234.28 \mu\text{m}$) than type 2 diabetics ($375.11 \mu\text{m}$), a mean difference of $140.82 \mu\text{m}$ (95% CI, 24.09 to 257.55), $t(41) = 2.43$, $p = 0.019$. Moreover, it was also revealed that patients who developed DRIL had a longer duration of diabetes (17 years) than those who hadn't (4.5 years), a mean difference of 12.46 years (95% CI, 10.59 to 14.33), $t(94) = 13.21$, $p < 0.001$.

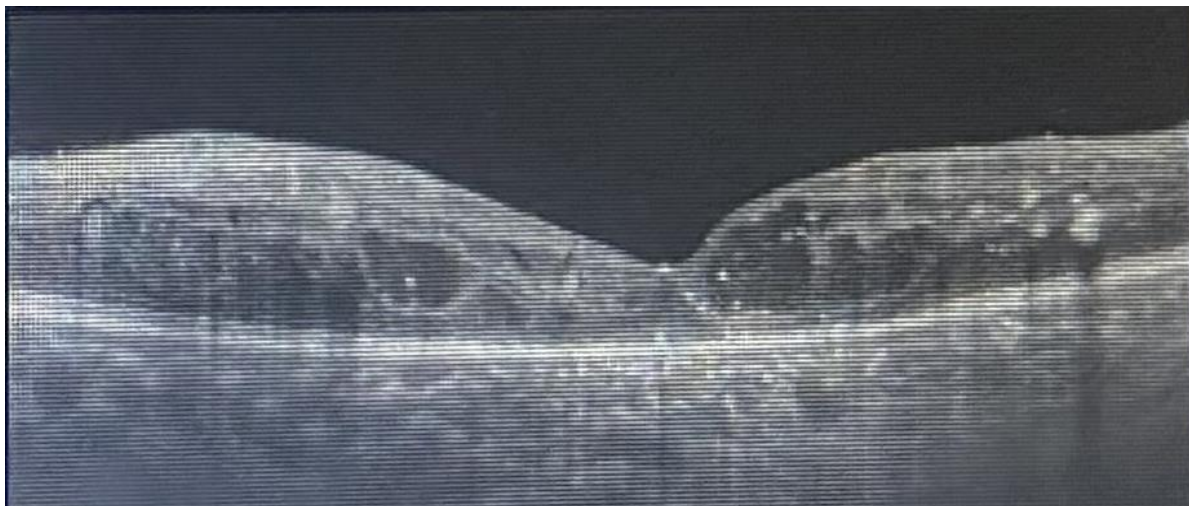


Figure 1. Identification of disorganization of retinal inner layers (DRIL) on optical coherence tomography (OCT).

Diabetic Macular Edema (DME) was found in 60 (62.5%) patients. There was a significant association between the existence of diabetic macular edema and DRIL ($p < 0.001$, Phi/Cramer's $V = 0.698$). Likewise, there was a strong positive

correlation (Pearson's) between central foveal thickness in micrometers and horizontal extent of DRIL in micrometers, which was statistically significant, $r = 0.66$, $n = 96$, $p < 0.001$ (Figure 2). Furthermore, One-way ANOVA revealed that there were

statistically significant differences in the means of central foveal thickness (micrometers) across the different visual acuity groups, $F(3, 92) = 87.64$, $p < 0.001$, partial eta squared = 0.741. A Tukey post hoc test revealed significant differences across all visual acuity groups (Table 1). Similarly, there was significant difference in the mean horizontal extent of DRIL (micrometers) across the different visual

acuity groups, $F(2, 40) = 69.05$, $p < 0.001$, partial eta squared = 0.775. A Tukey post hoc test revealed significant differences across all visual acuity groups (Table 1). One way ANCOVA revealed that there was significant difference in the mean horizontal extent of DRIL across different visual acuity groups while adjusted for mean central foveal thickness, $F(2, 39) = 29.42$, $p < 0.001$, partial eta squared = 0.601.

Table 1. The mean values of central foveal thickness and horizontal extent of DRIL across different visual acuity groups.

Visual acuity	Central foveal thickness (μm)			Horizontal extent of DRIL (μm)		
	No.	Mean	SD	No.	Mean	SD
6/6-6/9	43	208.88	37.33	0	-	-
6/12-6/18	27	293.18	32.07	17	210.58	57.70
6/24-6/36	14	370.35	77.11	14	374.71	88.54
6/60 or lesser	12	532.00	139.01	12	526.50	68.20
P value	p < .001			p < .001		

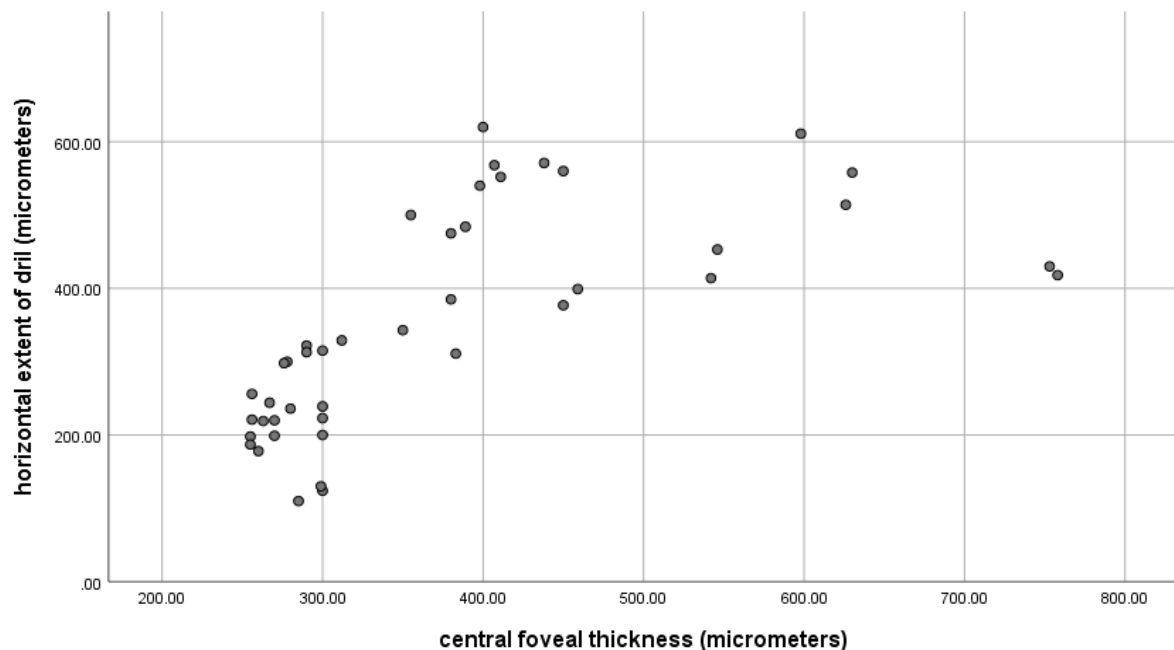


Figure 2. Scatter plot of horizontal extent of DRIL (micrometers) by central foveal thickness (micrometers)

Discussion:

Retinal inner layers play a crucial role in transmitting visual signals through neurons, and such transmission is dependent on the integrity of individual retinal layers. DRIL, as already described, disrupts the retinal inner layers and worsens retinal function. Research suggests that DRIL is characterized by significant morphological damage to Müller cells, rather than other retinal cells like microglia or neurons. Notably, Müller cells are the first to be impacted by intracellular edema in DME. Once activated, these cells release toxic substances that trigger a cascade of events, including inflammation, blood-retinal barrier disruption, glial dysfunction, and neuronal cell death, highlighting their crucial role in the disease's progression ⁶. DRIL has been extensively studied in a variety of retinal diseases like diabetic retinopathy, retinal vein occlusion, uveitis, and epiretinal membrane ^{10 11}. In our study, the frequency of DRIL was 44.8%. this is compatible with another study done in type 2 diabetics, where the frequency reported was 52.63% ⁶. In another study, done in both type 1 and type 2 diabetics, DRIL was found in 48.1% of the patients ¹². The slight discrepancy in prevalence rates may be due to differences in population demographics, study design, sampling methods or data analysis. Similarly, another small case-control study reported the frequency of DRIL as 16% ¹³. Our study also revealed that type 2 diabetics had more extensive DRIL than type 1 diabetics, but this finding was not observed in other studies. The plausible explanation for this could be that the propensity of type 2 diabetes to be diagnosed later in life, coupled with potential prolonged periods of inadequate glycemic control, is often cited as a contributing factor to the accelerated progression of retinal damage and further, because diabetic macular edema is more common in type 2 diabetes ¹⁴.

Chronicity plays a crucial role in the development of DRIL. Research reveals that patients with a longer disease duration

have a significantly higher incidence of DRIL. Our study also advocated this finding, as patients who developed DRIL had a longer duration of diabetes ¹. Although Disorganization of the Retinal Inner Layers (DRIL) has been extensively investigated as a surrogate biomarker for visual acuity in diabetic macular edema, our study yields a novel finding: a significant association between central foveal thickness (central subfield thickness) and the extent of DRIL in SD-OCT scans. This correlation is intriguing, as previous research suggested that sub retinal fluid and DRIL do not coexist due to DRIL's role as a marker of chronic diabetic macular edema. However, other studies have reported that persistent intraretinal cysts predict the development of DRIL. Given that increased central foveal thickness can result from sub retinal fluid, intraretinal cysts, or both, our findings imply that elevated central foveal thickness is linked to the development of DRIL ⁷.

Our study revealed that patients with extensive DRIL had poorer baseline visual acuity which is consistent with previous researches which have shown that the presence and extent of DRIL on OCT scans are strongly correlated with visual acuity outcomes in patients with DME. Patients with more extensive DRIL are less likely to achieve significant visual gains with treatment. The extent of Disorganization of the Retinal Inner Layers (DRIL) within the central 1mm of the fovea exhibits a robust correlation with visual acuity, even when adjustments are made for retinal thickness. Notably, early alterations in foveal DRIL extent have been found to be predictive of long-term visual outcomes. This association remains significant, irrespective of whether eyes exhibit reduced vision subsequent to edema resolution or maintain good vision despite the presence of concurrent edema. This suggests that DRIL extent is a critical determinant of visual acuity, independent of edema status ^{1 9}.

Anti-VEGF therapy has been shown to effectively reduce macular thickness and improve visual acuity in patients with diabetic macular edema (DME). However, response to treatment varies, with some patients experiencing significant improvement, while others show moderate or minimal response. Studies have found that patients with more extensive retinal layer disruption (DRIL) tend to have poorer treatment outcomes. Furthermore, some patients may not experience visual recovery despite successful DME treatment. The relationship between anti-VEGF therapy and DRIL is complex, with conflicting evidence on its impact. One study reported no significant change in DRIL even after multiple injections of anti-VEGF¹⁵. Recent research suggests that treatment with a DEX implant may improve DRIL, potentially by promoting Müller cell recovery⁷. This reveals that Müller cells are more resilient than neurons, and their morphological recovery can be detected as a restoration of DRIL. These findings support the notion that DRIL initially originates from Müller cell disruption, before involving bipolar cells, and highlight the potential for recovery. However, neuronal function and integrity may also be compromised later in the disease process, with limited potential for restoration. Thus, understanding the baseline characteristics that predict treatment response is essential, particularly in identifying patients at risk of poor outcomes.

Although this study provides valuable insights, its cross-sectional design constitutes a limitation. To elucidate the dynamic relationship between visual acuity and DRIL, as well as the responsiveness of DRIL to conventional macular edema treatments, longitudinal studies are warranted. These future investigations will enable the prediction of trends in visual acuity in relation to changes in DRIL, ultimately informing the development of more effective treatment strategies.

Conclusion:

This study validates the utility of DRIL as a potential biomarker. The extent of DRIL is correlated with severity of DME, making it a useful marker for disease progression. DRIL can be used to monitor treatment response in patients with DME allowing clinicians to adjust treatment strategies accordingly. Emerging evidence suggests that early intervention can potentially reverse DRIL, underscoring the importance of incorporating DRIL assessment into routine clinical practice to optimize patient outcomes.

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Effect of Peroperative Use of Heparinised Irrigating Solution on Postoperative Inflammation in Phacoemulsification

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Abstract:

Objective: To evaluate the effect of Heparin Sodium on postoperative inflammation following cataract surgery in adults.

Methods: A Quasi experimental study was conducted at Fauji Foundation Hospital, Rawalpindi during May to October 2023 which include one twenty (120) cases diagnosed with uncomplicated cataracts booked for phacoemulsification were randomized to Group 1 (heparinized solution) and Group 2 (Standard irrigating solution) using lottery method. Surgery was performed by single surgeon as per standard protocols. Patients were assessed preoperative and post-operative on day 1, day 7 and day 28 for visual acuity, intraocular pressure and detailed slit lamp examination to measure the AC cellular activity and AC flare in for all cases. SPSS-26 was used. Mean and standard deviations were computed for quantitative data, whereas, frequency and percentages were computed for qualitative data. The independent t-test was used to compare quantitative variables, while the chi-square/fisher exact test was used to evaluate qualitative variables. A P-value ≤ 0.05 was deemed as significant.

Results: The mean age of patients in the group 1 and group 2 were of 64.71 ± 9.69 years and 68.45 ± 9.69 years respectively. In both groups, most of the patients were female. However, no significant difference found in both groups in terms of baseline data. Significant difference in IOP, AC-cells and AC-flare was observed on day-1, day-7 and day-28 between both groups, as p-value was < 0.05 .

Conclusion: The study concluded that using heparin sodium as an anti-inflammatory drug could be effective in lowering post-operative inflammatory reaction. *Al-Shifa Journal of Ophthalmology 2025; 21(2): 50-55. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Recent estimates indicate that the prevalence of adult blindness is approximately 0.6% worldwide and 2.7% in Pakistan. Approximately 80% of these instances can be avoided.¹ One of the leading causes of reversible blindness worldwide is cataract, and cataract surgery accounts for a significant portion of each ophthalmic units' workload.² The ophthalmology community is debating the benefits and drawbacks of various procedures, including phacoemulsification, extra capsular cataract extraction, and manual suture-less cataract extraction. However, there is general agreement that all procedures should have minimal postoperative inflammation following surgery.³

One major factor contributing to delayed vision recovery following cataract surgery

is postoperative inflammation. Another consequence to which eyes with an elevated inflammatory response are vulnerable is cystoid macular edema, which may or may not lead to irreversible vision loss⁴. Additionally, eyes with an inflammatory reaction are more likely to experience posterior capsular opacification, a delayed postoperative consequence.⁵ Over 50 years after the first intraocular lens (IOL) was implanted, research is still being conducted to make the IOLs more biocompatible and reduce postoperative inflammation.⁶ Because of its anti-inflammatory qualities, heparin is utilized in pediatric cataract surgery as coatings for intraocular lenses and as irrigating solutions to lessen inflammation after surgery.⁷ Heparin possesses anti-proliferative and anti-inflammatory properties. Apart from its anticoagulant properties, heparin has been demonstrated to suppress fibroblast activity and prevent fibrin formation following eye surgery.⁸ There is less post-operative inflammation in eyes implanted with heparin-coated lenses, according to a few studies.^{9,10} Nevertheless, no comparable research has been reported in the Pakistani community, which is known to have darker skin and be more susceptible to post-operative inflammation.¹⁰ In this study, we assessed how adding heparin sodium to the irrigating solution during cataract surgery affected the procedure.

Methodology:

This Quasi experimental study was conducted in the department of ophthalmology at Fauji Foundation hospital, Rawalpindi, from May to October 2023 after the approval of research protocol from Ethical Review Committee of the hospital [No. 685/RC/FFH/RWP]. Using a consecutive non-probability sampling technique, 120 cases of either gender, older than 50, with simple cataracts who were scheduled for phacoemulsification were chosen. All patients had good glycemic and hypertensive control. They were given a hospital number, and the procedure was

performed with their informed consent. Preoperative examinations include visual acuity assessment by Log Mar chart, intraocular pressure measurement by Goldman's applanation tonometry, detailed slit lamp examination carried out to measure the AC cellular activity and AC flare were carried out for all cases. Exclusion criteria were history of ocular pathology like advanced glaucoma, uveitis, high myopia, pseudo exfoliation, complicated cataracts, subluxated lens, previous ocular surgery, severe diabetic retinopathy, Fuchs' endothelial dystrophy and any ocular surface disease. Brunescant cataracts were also excluded because of prolonged surgical time. Patients were randomized to group 1 (heparinized solution) and group 2 (Standard irrigating solution) using lottery method. Patients allocated to group 1 received anterior chamber irrigation with heparin sodium (10IU/1ml) in standard irrigating solutions during phacoemulsification and group 2 received standard irrigating solutions. All procedures were carried out by a single surgeon using topical anesthetic and the conventional phacoemulsification technique. All cases were uneventful. At the conclusion of the procedure, hydrophobic acrylic foldable intraocular lenses were placed in each patient. Postoperatively, potent topical antibiotic drops were prescribed along with Prednisolone acetate 1% eye drops six times a day for 4 weeks. Patients were assessed pre-operatively and postoperatively on day 1, day 7 and day 28 which included VA, IOP, AC cellular activity and AC-flare as per method as mentioned above. According to SUN (standardization of uveitis nomenclature), anterior chamber flare was evaluated as follows: 0 = no flare, 1 = mild and barely perceptible flare, 2 = moderate flare with clear iris details, 3 = noticeable flare with blurry iris details, and 4 = extreme flare with severe fibrinous exudates per high-power field. AC Cellular activity was graded as: 0 = <1 cell, +0.5= 1-5 cells, +1=

6-15 cells, +2= 16-25cells, +3= 26-50 cells, +4= >50 cells per high power field as per SUN. During each visit, three measurements were taken to determine the degree of anterior chamber inflammation, and the average of these measurements was noted as the final value. All readings were taken by single observer to prevent interobserver variability. Data was entered and analyzed with the help of SPSS-26. Mean and Standard Deviation was calculated for quantitative variables while, frequency and percentages were calculated for qualitative variables. Qualitative variables were compared using chi-square/Fisher's exact test and quantitative variables were compared using independent

t-test. A P-value ≤ 0.05 was considered as significant and confidence intervals at 95% were calculated.

Results:

There were 120 patients in all (60 in the group 1 and 60 in the group 2). Patients in the group 1 were 64.71 ± 9.69 years old, whereas those in the group 2 were 68.45 ± 9.69 years old. The majority of patients in both groups suffered from hypertension and diabetes. Since the p-value was more than 0.05, there was no significant difference between the two groups in terms of baseline data, as shown in table 1.

Table 1: Baseline data of the Patients

Baseline Data	Group 1	Group 2	P-value
Age (mean \pm SD)	64.71 ± 9.69	68.45 ± 9.69	0.528
Gender n(%)			
• Male	04 (6.6%)	2 (3.3%)	0.402
• Female	56 (93.3%)	58 (96.6%)	
Co-morbid (%)			0.97
• Diabetes Mellitus	11 (18.3%)	10 (16.6%)	
• Hypertension	16 (26.6%)	14 (23.3%)	
• Ischemic heart disease	05 (8.3%)	04 (6.6%)	
• DM & HTN	16 (26.6%)	17 (28.3%)	
• DM, HTN & IHD	02 (3.3%)	03 (5%)	

None of the patients experienced any intraoperative complications. The p-value was less than 0.05, indicating a significant difference between the two groups on days 1, 7, and 28. Further, there was no

significant difference in VA between group 1 and group 2 pre-operatively and postoperatively (day-28), as shown in table 2 and figure 1.

Table 2: Anterior Chamber Cellular Activity in the Study and Control Groups

Follow-up	Parameters	Groups		P-value	95% Confidence	
		Study Group	Control Group		Lower limit	Upper limit
Pre-Operative	VA	0.8±0.25	0.8±0.21	0.752	-0.070	0.096
	IOP	13.98 ± 2.87	13.183 ±	0.075	-0.083	1.68
	AC-Cells	0.03 ± 0.18	2.87	0.156	-0.12	0.079
	AC-Flare	0	0	0.081	-0.106	0.006
Day-1	IOP	13.06 ± 4.41	13.08	0.985	-1.75	1.71
	AC-Cells	0.62±0.39	±4.42	0.000	-2.05	-1.69
	AC-Flare	0.60 ± 0.49	2.49 ± 0.56	0.000	-0.65	-0.310
			1.08 ± 0.46			
Day-7	IOP	13.28 ± 3.40	13.43	0.805	-1.34	1.04
	AC-Cells	0.44 ± 0.73	±3.22	0.000	-1.36	-0.88
	AC-Flare	0.433± 0.49	1.56± 0.61	0.044	-0.43	-0.084
			0.69 ± 0.46			
Day-28	VA	0.2± 0.13	0.2± 0.09	0.810	-2.5	0.036
	IOP	11.83 ± 2.56	13.28 ±	0.013	-0.258	-0.317
	AC-Cells	0.22 ± 0.40	3.54	0.000	-0.762	-0.38
	AC-Flare	0.433± 0.49	0.80 ± 0.61	0.000	-0.39	-0.15
			0.69±0.46			

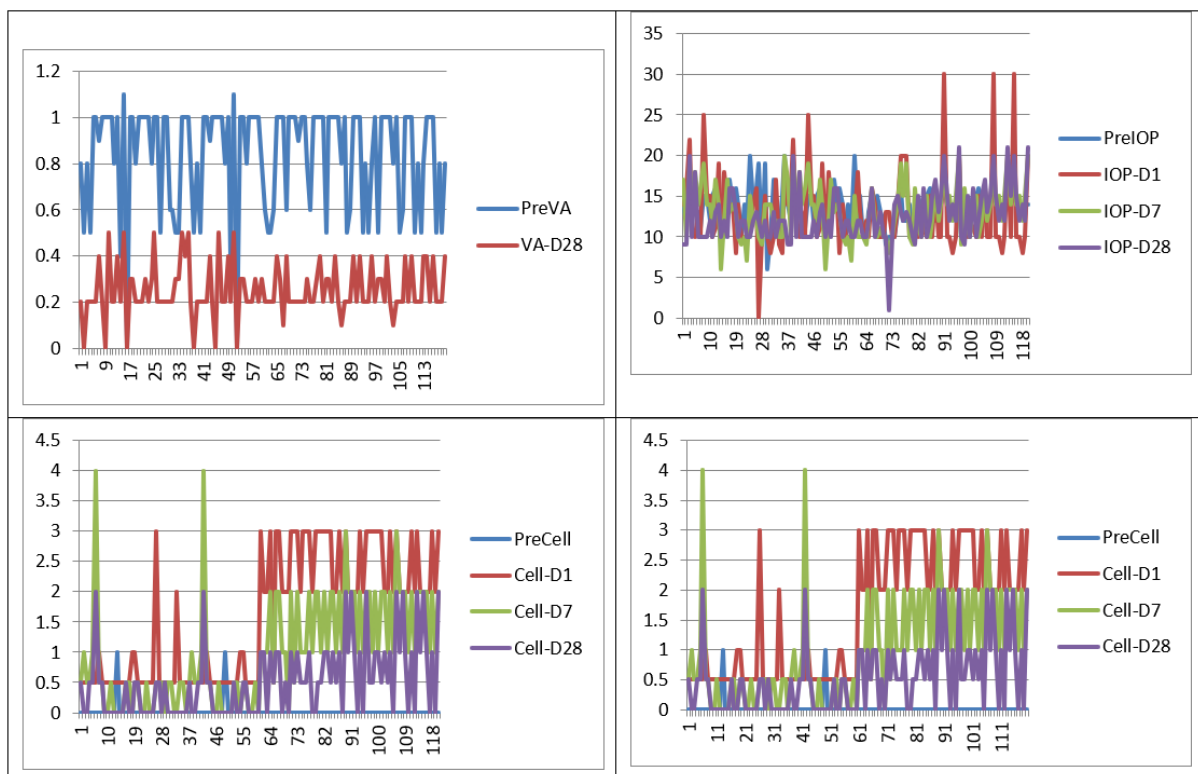


Figure 1: Anterior Chamber Cellular Activity in the Study and Control Groups

Discussion:

Globally, age-related cataracts are the most common cause of progressive visual loss. Worldwide, cataract surgery accounts for the majority of eye units' workload and is a significant medical expense. In terms of improved quality of life, it is among the most economical public health interventions.¹¹ The key factors influencing the success of contemporary cataract surgery are vision quality and early visual rehabilitation. These two metrics are thereafter reliant on post-operative inflammation and surgical procedure problems.¹²

The coagulation and fibrinolytic pathway may be disrupted by any abnormality in the blood–aqueous barrier, which could be brought on by intraocular inflammation, high intraocular pressure (IOP) prior to surgery, or severe eye manipulation during surgery.¹³

It has been suggested that heparin is a good option for lowering the inflammatory response following cataract surgery. Heparin-coated IOLs and heparin solution added to irrigating solutions during phacoemulsification are two examples of its use. During phacoemulsification, we added 10 IU/ml of heparin sodium to a balanced salt solution for irrigation. An irrigating solution without heparin was used during surgery on a parallel group of patients. Visual acuity, intraocular pressure, AC-cells, and AC-flare did not differ significantly before surgery; however, we discovered a statistically significant difference in intraocular pressure, AC-cells, and AC-flare between the two groups up to the 28th day after surgery, but no significant difference in visual acuity between the two groups. The study's findings are consistent with those previously documented in situations involving IOL implantation and phacoemulsification. Kruger et al. discovered that individuals who received heparin-supplemented irrigating fluid had a reduced inflammatory cellular response in the anterior chamber.¹⁴ In a study

conducted by Kruger et al. and Kohnen et al., the anti-inflammatory effect of heparin lasted until the first and third postoperative days, respectively.^{14,15} The number of participants in our study was lower than in prior studies, which is one of the two main differences between the two. Therefore, additional studies and trials with a bigger sample size are required to further support the findings.

In contrast to our study, these investigations measured the cells and flare in the anterior chamber using a laser flare and cell photometer.

According to research, heparin sodium is a workable way to prevent inflammation by inhibiting the complement pathways, inhibiting the formation of several complement factors, interfering with terminal cell lysis.¹⁶ In addition, heparin can interact with pro-inflammatory cytokines and chemokines,¹⁷ preventing these pro-inflammatory molecules from interacting with their specific receptors. Some evidence shows that heparin interferes with the adhesion of leukocytes to the endothelium.¹⁷ The group 1 improved significantly after a day compared to the group 2 because of the inflammatory process and AC cellular activity were under control. Within 24 hours, all cases in group1(with heparin sodium) showed a considerable improvement in vision without any complications or irritation. By lowering post-operative inflammation, Heparin Sodium serves as an agent for early visual rehabilitation in addition to being appropriate for lowering cellular activity following phacoemulsification.¹⁸

In general, heparin is used as an anticoagulant, but it also possesses anti-inflammatory properties.¹⁹ By suppressing fibroblastic activity, it prevents fibrous responses during intraocular surgery.²⁰ Because of these special qualities, researchers are using heparin in surface-modified IOLs for cataract surgery.^{20,21} In a similar view, Bayramlar and associates came to the conclusion that heparin added to the irrigating solution during surgery

reduces late inflammatory problems and postoperative fibrinous response. In their study, Ihsan Ç and colleagues came at the same conclusion.²²

Follow-up for longer period wasn't a part of this study, therefore, long-term impact on complications like cystoid macular edema (CME) and posterior capsular opacification (PCO) in adult cataract patients could not be assessed as they are not the main objectives of study. Further small size did not allow us to do adjustments for multiple comparisons, as a smaller sample may give a result that may not be sufficiently powered to detect a difference between the groups and the study may turn out to be falsely negative leading to a type II error. Nevertheless, our study has shed light on the potential significance of heparin in reducing the post-operative inflammation, which can inspire our colleagues to create additional studies to address the shortcomings of our study.

Conclusion:

In the phacoemulsification process, heparin sodium was added to the infusion bottle as an anti-inflammatory. The study concluded that using heparin sodium as an anti-inflammatory drug could be effective in lowering post-operative inflammation and reaction.

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