

Clinical features and surgical outcomes of complications of proliferative diabetic retinopathy in young adults with type 1 diabetes mellitus versus type 2 diabetes mellitus - A comparative observational study

Karthik Kumar, Girish Baliga, Naresh Babu, Renu P Rajan, Gautam Kumar, Chitaranjan Mishra, Chitra R¹, Kim Ramasamy

Purpose: To evaluate the clinical profile, visual outcomes, and complications among young adult patients with type 1 diabetes mellitus (insulin-dependent DM-T1DM) in comparison with patients with type 2 diabetes mellitus (T2DM) undergoing vitrectomy for complications of proliferative diabetic retinopathy (PDR). **Methods:** A retrospective review of patients between 18 and 45 years with T1DM undergoing vitrectomy for complications of PDR between June 2017 and June 2019, with a minimum follow-up of 12 months. Consecutive patients between 30 and 45 years with type 2 diabetes (non-insulin-dependent DM-T2DM) who underwent vitrectomy for the same indications were retrospectively enrolled as the control group. **Results:** There were 42 eyes (28 patients) in the T1DM group and 58 eyes (47 patients) in the T2DM group. The average age at operation was 35.9 ± 6.88 years and 39.8 ± 3.03 years, respectively ($P < 0.001$). At the end of follow-up, the mean logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) improved from 1.53 ± 0.55 to 1.30 ± 0.93 (P value 0.07) in the T1DM group and from 1.59 ± 0.46 to 1.00 ± 0.78 in the T2DM group ($P = 0.0001$). The rate of the primary and final reattachment was 76.2% and 88.1% in the T1DM group and 84.5% and 96.6% in the T2DM group. Preoperative macular tractional retinal detachment (MTRD) and neovascular glaucoma (NVG) in both the groups, chronic kidney disease (CKD) and lack of preoperative Pan retinal photocoagulation (PRP) in the T1DM group, hypertension (HTN) and, resurgery in the T2DM group, were risk factors for poor vision at the final follow-up. **Conclusion:** The visual and anatomic outcomes were poorer in the T1DM patients which could be due to the longer duration of diabetes with worse glycemic control, associated comorbidities like CKD, and a higher incidence of MTRD.

Key words: Proliferative diabetic retinopathy, type 1 diabetes mellitus, vitrectomy

Diabetic retinopathy (DR) is the cause of blindness in approximately 2.5 million of the estimated 50 million blind people in the world.^[1] India with 77 million diabetic patients as per estimates, second only to China, is likely to face an increasing cascade of microvascular complications of which DR is one of the most frequent.^[2] There are 1.1 million children and adolescents with type 1 diabetes mellitus (T1DM) worldwide and 132,600 new cases are added each year in people aged 0–19 years.^[3] T1DM, which could be autoimmune or idiopathic, is on the increase in India with a 3–5% increase/year.^[4] The Diabetes Atlas 2017 estimates that there are 128,500 children and adolescents with diabetes in India.^[5] It is believed that over 80% of the patients with T1DM have some form of DR which could be sight-threatening when the duration of diabetes is over 15 years.^[4,6]

Twenty-five percent of diabetes-related vision loss stems from complications of proliferative diabetic retinopathy (PDR)

which is associated with new vessel formation on the retina and optic disk as a consequence of hypoxia and capillary occlusion.^[7] The age at onset of DM is considered an important factor in the development and progression of DR and its complications like vitreous hemorrhage (VH), tractional retinal detachment (TRD), and severe fibrovascular proliferation which might occur rapidly in the early-onset of the disease.^[8] TRD remains one of the most feared complications of DR.^[9] Vitrectomy for PDR in young patients is often challenging due to the broad vitreoretinal adhesion and severe active fibrovascular proliferation and a higher rate of postoperative complications like recurrent VH, recurrent retinal detachment, and neovascular glaucoma (NVG).^[10–12] The outcomes of diabetic vitrectomy in older patients have been widely analyzed.^[13–15] Only a few studies have analyzed the outcomes of surgery in young diabetic patients with PDR.^[10–12] The previous studies have investigated possible predictors for DR in people with

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Cite this article as: Kumar K, Baliga G, Babu N, Rajan RP, Kumar G, Mishra C, et al. Clinical features and surgical outcomes of complications of proliferative diabetic retinopathy in young adults with type 1 diabetes mellitus versus type 2 diabetes mellitus - A comparative observational study. Indian J Ophthalmol 2021;69:3289-95.

Access this article online

Website:
www.ijo.in

DOI:
10.4103/ijo.IJO_1293_21

Quick Response Code:



Department of Vitreo-Retinal Services, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, ¹Department of Biostatistics, Aravind Medical Research Foundation, Madurai, Tamil Nadu, India

Correspondence to: Dr. Girish Baliga, Medical Consultant, Department of Vitreo-Retinal Services, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai, Tamil Nadu, India. E-mail: irish192@gmail.com

Received: 18-May-2021

Revision: 30-Aug-2021

Accepted: 28-Sep-2021

Published: 29-Oct-2021

T1DM, however, there is an unmet need to evaluate the surgical outcomes following vitrectomy in T1DM patients.^[3,16] The present study aims to evaluate the clinical profile, visual outcomes, and complications among young adult patients with T1DM requiring vitrectomy for the complications of PDR.

Methods

This was a retrospective study done at a tertiary eye care center in South India. The medical records of the consecutive patients who underwent pars plana vitrectomy (PPV) secondary to PDR-related TRD and VH from June 2017 to June 2019 and having a minimum follow-up of 12 months were included in the study. All the patients were operated on by three senior vitreoretinal surgeons (Dr NBK, Dr KK, Dr RPR). The study was conducted with the approval of the institutional review board (Registration No. ECR/182/INST/TN/2013/RR-19 dated 12.05.2020) and adhered to the tenets of the Declaration of Helsinki. The patients were classified as either having T1DM (T1DM group) if DM was diagnosed before 30 years of age associated with the requirement for insulin from the time of diagnosis or T2DM (T2DM group) if the patients were diagnosed after 30 years of age and were on oral hypoglycemic agents with or without the need for exogenous insulin.

The surgical indications included (1) Non-clearing dense VH of more than 3 months duration with minimal TRD (group I), (2) Progressive fibrovascular proliferation (FVP) with extramacular TRD (EMTRD) (group II), (3) Tractional macular detachment (MTRD) (group III), (4) Combined traction and rhegmatogenous retinal detachment (CRD) (group IV). The anatomical success in the eyes undergoing surgery for TRD was defined as a flat retina without subretinal fluid in the posterior pole, i.e., between the vascular arcades. The anatomical success in the eyes undergoing surgery for VH was defined as resolution of vitreous hemorrhage and a presence of a clear media with a flat retina without subretinal fluid in the posterior pole. All cases with a history of previous vitreoretinal surgical intervention or having less than 12-month follow-up were excluded. In patients with preoperative visually significant cataract, phacoemulsification with intraocular lens replacement was performed prior to vitrectomy by a cataract surgeon. Preoperative intravitreal injection of bevacizumab 1.25 mg was performed 5–7 days before the surgery in those cases with active FVP with a florid neovascular component which was felt to be at high risk for severe intraoperative bleeding. All the patients underwent 23G vitrectomy using the Alcon Constellation vitrectomy machine (Alcon Laboratories, Fort Worth, TX) with a noncontact viewing system RESIGHT 700 (Carl Zeiss Meditec AG, Oberkochen, Germany). After a triamcinolone-assisted core vitrectomy for identifying posterior hyaloid, the membrane was isolated either from the periphery using an “Outside in” approach or in broadly adherent posterior hyaloid with unidentifiable tissue planes, an “inside out” approach starting from the optic disk was used. A fibrovascular membrane dissection was performed using a combination of one or more of the following instruments, i.e., a cutter, end-gripping forceps, and microscissors. The bimanual technique was used as and when required depending upon the complexity of the membranes. The bleeders were controlled by raising infusion pressure or by endodiathermy in severe cases. Perfluoro-n-octane (PFO) liquid was used as a third hand for the dissection of adherent membranes and also for stabilizing the retina during the step of Brilliant blue G (BBG)-assisted internal limiting membrane (ILM)

peeling which was performed in all the patients. Vitreous base shaving with scleral depression was performed in all the cases. The reason for doing this was to (1) ensure a near-complete vitrectomy, (2) ensure the complete removal of clotted hemorrhage from the inferior peripheral vitreous, which may act as a nidus for post-op recurrent dispersed VH. After the fluid–air exchange, all breaks were lasered, and a 360° peripheral laser was performed in all the cases, which helps in the prevention of recurrent neovascularization and VH in these eyes. Silicone oil was used as a tamponade in the cases with retinotomies, in the eyes with residual traction due to fibrovascular membranes with persistent subretinal fluid intraoperatively, and if the poor vision in the fellow eye necessitated postoperative clear media and the need for instant visual rehabilitation, which would be difficult to achieve with gas tamponade. Chart review was used to collect data for all patients. The variables collected included sex, age, duration of diabetes, history of other concurrent systemic diseases like hypertension, coronary artery disease, and renal status. Chronic kidney disease (CKD) or diabetic nephropathy (DN) was defined as the estimated glomerular filtration ratio (eGFR) <60 mL/min/1.73 m² using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The best-corrected visual acuity (BCVA) was measured using Snellen’s chart. The Snellen’s acuity was then converted to logarithm of the minimum angle of resolution (logMAR) equivalent. The other data collected included preoperative or most recent hemoglobin A1c (HbA1c), systolic and diastolic blood pressures on the day of the surgery, preoperative pan-retinal photocoagulation, concurrent rhegmatogenous retinal detachment (RRD), concurrent VH, macula status at the time of surgery, preoperative bevacizumab usage, instrument gauge, use of tamponade agents, postoperative course, and complications. The outcome measures were postoperative BCVA at 1, 3, 6, and 12 months, anatomic success after the first surgery and at the final follow-up, and incidence of postoperative complications.

Statistical analysis

Descriptive statistics were presented with frequency and percentage for categorical data. The mean and standard deviations (SD) were used for continuous parametric data while median and interquartile ranges (IQR) were used for non-parametric data. The unpaired *t*-test was used to find out the significant difference between the two groups. The risk factors for poor final visual acuity were evaluated by linear regression; the statistical significance was set at the *P* = 0.05 level. All of the statistical tests were two-sided at the 5% level and were performed using STATA 14.

Results

Preoperative patient characteristics

Forty-two eyes of 28 patients (men 53.6% and women 46.4%) were included in the T1DM group; 58 eyes of 47 patients (men 70.2% and women 29.8%) were included in the T2DM group. The preoperative baseline characteristics of both groups are depicted in Table 1. The mean age at surgery was 36.7 years (range 19–45 years) and 40.5 years (31–45 years) in the two groups, respectively. The mean duration of diabetes was 12 years (range 1–22 years) and 7.8 years (range 1–20 years) in the two groups, respectively. The mean age at the diagnosis of DM was 24.7 and 32.3 years in the two groups, respectively. Out of the 28 patients, 9 patients were diagnosed with T1DM

Table 1: Baseline features of T1DM and T2DM patients who underwent pars plana vitrectomy

Clinical features	T1DM eyes, n=42 (%)	T2DM eyes, n=58 (%)	P
Patients	28	47	
Male	15 (53.6)	33 (70.2)	0.16
Female	13 (46.4)	14 (29.8)	0.16
Mean age at surgery±SD, years	36.66±6.88	40.46±3.03	<0.001*
Mean age at diagnosis±SD, years	24.73±8.44	32.31±6.40	<0.001*
Duration of diabetes, ± SD, years	11.96±5.24	7.83±5.59	<0.001*
Mean length of follow-up (months)	14.62±5.81	15.87±7.65	0.373
Systemic hypertension	14/28 (50.00)	22/47 (46.80)	0.461
Systolic blood pressure (mmHg)	143.65±23.16	141.89±22.27	0.640
Diastolic blood pressure (mmHg)	83.36±11.44	82.06±11.39	0.531
Chronic kidney disease	12 (42.9)	5 (10.6)	<0.001*
Mean serum creatinine levels	1.80±1.83	1.17±1.01	0.033*
Ischemic heart disease	3 (10.7)	3 (6.4)	0.405
Mean preoperative HbA1c (range) gm%	9.29±2.95 (4-14.8)	9.18±1.98 (5.9-14.7)	0.682
Phakic eyes with clear lens	25 (59.5)	41 (70.7)	0.25
Eyes with cataract	16 (38.1)	17 (29.3)	0.36
Pseudophakic eyes	1 (2.4)	0 (0.0)	0.11
Mean preoperative BCVA±SD	1.53±0.55	1.59±0.46	0.538
Preoperative IOP (mmHg)	15.80±3.83	15.15±2.51	0.33
Indication			
Macular TRD	21 (50)	21 (36.2)	0.17
Extramacular TRD	6 (14.3)	12 (20.7)	0.40
Combined tractional rhegmatogenous RD	4 (9.5)	7 (12.1)	0.68
Dense VH with fibrovascular proliferation +/- TRD	11 (26.1)	18 (31.1)	0.59
Quadrant of fibrovascular proliferation			
1 Quadrant	3 (7.1)	8 (13.8)	0.78
2 Quadrant	3 (7.1)	9 (15.5)	0.43
3 Quadrant	13 (31)	16 (27.6)	0.34
4 Quadrant	23 (54.8)	25 (43.1)	0.30
Preoperative pan-retinal photocoagulation	31 (73.8)	33 (56.9)	0.13
Preoperative bevacizumab	7 (16.7)	6 (10.3)	0.37

*P<0.05 Statistically significant

before the age of 18 years (32.1%) with the youngest age at diagnosis being 2 years, 67.8% (19/28) were diagnosed with T1DM after the age of 18 years. There was a statistically significant difference between the two groups in terms of the presence of CKD. Preoperative intravitreal bevacizumab was used in the T1DM group in seven eyes (16.7%) with highly vascular membranes, 5–7 days prior to the surgery, and in six eyes (10.3%) in the T2DM group. In the T1DM group, 21/42 eyes (50%) had MTRD whereas, in the T2DM group, it constituted 36.2% of the eyes. In the T1DM group, 3 and 4 quadrants FVP was seen in 31% and 54.8% of the eyes, which was more than that in the T2DM group indicative of the more extensive nature of proliferation in the T1DM group.

Visual and anatomical outcomes

At the end of the follow-up, the mean BCVA (logarithm of the minimum angle of resolution) improved from 1.53 ± 0.55 to 1.30 ± 0.93 ($P = 0.07$) in the T1DM group and from 1.59 ± 0.46 to 1.00 ± 0.78 in the T2DM age group ($P = 0.0001$). The anatomic and functional outcomes following surgery are described in Table 2. Postoperatively, the BCVA improved in 26 eyes (61.9%), remained stable in 5 eyes (11.9%), and became worse in 11

eyes (26.2%) in the T1DM group. In the T2DM group, the BCVA improved in 44 eyes (75.7%), remained stable in 5 eyes (8.6%), and became worse in 9 eyes (15.5%). On comparison of the pre- and postoperative BCVA improvement based on the preoperative indications, in the T2DM group, all eyes except those with MTRD had statistically significant improvement in vision, whereas, in the T1DM group, only the eyes with dense VH with minimal TRD and eyes with CRD had the same outcome [Table 3]. The retina was reattached in 32 eyes (76.2%) after primary surgery and the final attachment rate was 88.1% without any further surgical intervention in the T1DM group. In the T2DM group, the primary attachment rate was 84.5% and the final attachment rate was 96.6%. The total procedures at the end of 1 year in the T1DM group were 80 with a mean of 1.9 ± 0.9 procedures per patient, and in the T2DM group, the total number of procedures was 117 with a mean of 2.0 ± 0.7 procedures per patient.

Complications

Ten eyes in the T1DM group (23.8%) had recurrent detachment, out of which 5 eyes (11.9%) had successfully attached the retina after resurgery, 3 eyes had neovascular glaucoma, 2 eyes had

gross disk pallor post-multiple resurgeries, hence, these 5 eyes were not considered for further intervention in view of the poor prognosis. In the T2DM group, 2 eyes had detached retina at the final follow-up. All of these eyes also had neovascular glaucoma, and hence, were considered poor candidates for resurgery. Eight of the 42 eyes had NVG (19%) in the T1DM group compared with 7 of the 58 eyes (12.1%) in the T2DM group. A significant VH requiring vitrectomy was seen in 9.5 and 15.5% in the two groups, respectively. Secondary glaucoma controlled with anti-glaucoma medication was seen in 2/42 eyes (4.8%) and 11/58 eyes (19%) in the T1DM and T2DM groups, respectively. Cataract formation was seen in 17/42 eyes (40.5%) and in 35/58 (60.3%) eyes in both groups. Optic disk pallor was seen in 76.2 and 70.7% of the eyes in both groups.

Discussion

It has been shown that over half of the people with young-onset diabetes, regardless of type, have retinopathy within 10–12 years of diabetes duration which increases to nearly all patients with T1DM after two decades of the disease.^[6,17] DR from T1DM has been reported to behave more aggressively with extensive FVP and TRD.^[10] The disease duration has been identified as a significant risk factor for severe disease with the rates of PDR increasing from 1.2% in the patients with T1DM for <10 years to 67% in those diagnosed with diabetes for 35 years or more.^[18] Worldwide, the incidence of type 1 diabetes is 15 per 100,000 people and a prevalence of 9.5% suggesting an upward trend that makes diabetic vitrectomy not a rare event anymore in the T1DM population as was previously thought.^[16] Since Asian Indians tend to get type 2 diabetes at an earlier age and as the proportion of patients with T1DM above 30 years of age at diagnosis is increasing to as high as 50% in some studies,^[3] it becomes imperative to study the surgical outcomes following diabetic vitrectomy in this population. In this present study, we chose 45 years of age as the cutoff point to include young diabetic patients with complications of PDR because studies have shown diabetes onset <45 years of age to be associated with an increased risk of DR and its complications like severe FVP and TRD.^[19] Both groups also had a statistically significant age difference between the mean age at the diagnosis and surgery suggesting that both groups were indeed representative of the clinical profile of advanced PDR in their respective groups.

Young diabetic patients with PDR present unique challenges which can affect the surgical outcomes adversely.^[10,11] Younger patients with PDR commonly have a higher grade of FVP and more extensive TRD with florid, active neovascularization in the membrane which can cause uncontrollable hemorrhage during surgery. Second, the posterior hyaloid is almost completely attached to the retina, which makes induction of posterior vitreous detachment (PVD) fraught with the risk of inducing iatrogenic retinal breaks during the surgery. The complications following vitrectomy like recurrent VH, postoperative NVG, and recurrent retinal detachment also tend to be higher in young patients with PDR.^[10,11]

Though DR is more common in T1DM as compared to T2DM, systemic risk factors like hypertension and microalbuminuria have been found to be more in T2DM.^[20] However, we found a significantly higher proportion of patients with CKD in the T1DM group. Higher mean HbA1c, longer duration of DM with earlier onset in the T1DM group could have a bearing on the higher incidence of nephropathy.

Although surgical outcomes of PPV for complications of PDR have been described in detail, the literature regarding the outcomes in young patients with early-onset diabetes is limited.^[10,12] In the era of microincision vitrectomy surgery, overall, the rates of final retinal reattachment have ranged from 67 to 100% with the rate of resurgery having fallen to 6–31%.^[9,14] The rate of the final reattachment was 88.1% and 96.6% in our two groups, respectively. This could partly be explained by the higher proportion of complex detachments with macular involvement in the T1DM group. Secondary retinal detachment has been reported in up to 36% of the cases after primary vitrectomy for PDR.^[14] Resurgery for recurrent retinal detachment was needed in 23.8% of the patients in the T1DM group and in 15.5% of the patients in the T2DM group which is more than the recurrent RD rate of 13.2% noted by Huang *et al.*^[10] In the study by Huang *et al.*, the mean HbA1c was 7.90%, and in the current study, the HbA1c was 9.29 and 9.18% in the T1DM and T2DM groups, respectively, which reflects the uncontrolled nature of the disease in our patients, silicone oil tamponade was needed in 38.2% of the eyes in their study, however in the current study, 85.71% of the eyes in the T1DM group and 87.93% of the eyes in the T2DM group, needed silicon oil tamponade.^[10] Probably, the complexity of the TRD was more severe in the eyes included in the current study needing silicone oil tamponade instead of gas tamponade which could be possible explanations for the increased rate of recurrent RD in the current study. Studies show advantages in the eyes undergoing vitreoretinal surgery with additional ILM peeling in comparison to those eyes without ILM peeling.^[21,22] These advantages include decrease in epiretinal membrane formation, macular edema, and need for additional surgeries postoperatively.^[21,22] Additionally, ILM peeling helps in identifying second membranes in complex detachments, and ensures completeness of the PVD induction. In our series, intraoperative BBG-assisted ILM peeling was done in all the eyes.

Studies assessing the visual outcomes for TRD repair typically report postoperative visual acuity $\geq 20/40$ in 11–29%, 20/200 in 36.2–62.5% of the cases, and ambulatory vision $\geq 20/400$ in 57.6–79.1%.^[7,9,13,19] Our series showed 14.3% of the patients in the T1DM group and 24.1% of the patients in the T2DM group achieved a BCVA of 20/40 (0.3 logMAR) or better at the final follow-up. 52.4 and 55.2% of the patients in both groups, respectively, achieving BCVA of 20/200 (1.0 logMAR) or better. The ambulatory vision ($\geq 20/400$) was achieved in 66.7 and 79.3 %, respectively, in the two groups. The proportion of patients with PL and No PL vision were also higher in the T1DM group (21.4%) as compared to the T2DM group (6.9%) which was suggestive of a relatively favorable outcome in the postoperative vision in the T2DM group.

Postoperative vitreous hemorrhage (POVH) has been reported in 16–55% of the cases in recent times, however, VH typically only requires repeat vitrectomy in 5–10% of the total cases.^[14] Additional vitrectomy for POVH was required in 9.5% (4/42) in the T1DM group and 15.5% (9/58) in the T2DM group in our study. The literature is inconsistent on the opinion regarding Intravitreal Bevacizumab (IVB) injection and postoperative functional outcomes. Choovuthayakorn *et al.* found that adjuvant IVB either before or at the end of PPV had no significant association with the final visual outcomes.^[15] Chen *et al.*^[11] found intravitreal ranibizumab pretreatment to be a safe and effective adjunct to vitrectomy in reducing intraoperative and early post-vitrectomy bleeding in young

Table 2: Anatomic and functional outcomes following vitrectomy

Parameter	Number of eyes (%)		P
	T1DM	T2DM	
Primary reattachment with single surgery	32 (76.1)	48 (84.5)	0.42
Final attachment	37 (88.1)	56 (96.6)	0.13
Visual outcomes			
Postoperative BCVA			
≥20/40	6 (14.3)	14 (24.1)	0.21
≥20/200	22 (52.4)	32 (55.2)	0.78
≥20/400	28 (66.7)	46 (79.3)	0.16
<20/400	14 (33.3)	12 (20.7)	0.16
Improved	26 (61.9)	44 (75.7)	0.14
Stable	5 (11.9)	5 (8.6)	0.60
Worsened	11 (26.2)	9 (15.5)	0.20
PL and NO PL	9 (21.4)	4 (6.9)	0.04*
Mean postoperative BCVA±SD-at final follow-up	1.30±0.93	1.00±0.78	0.09
Postoperative IOP (mmHg)	17.07±11.67	16.86±4.84	0.91
Complications			
Postoperative vitreous hemorrhage	5 (11.9)	11 (19)	0.33
Vitreous hemorrhage requiring lavage	4 (9.5)	9 (15.5)	0.36
Recurrent retinal detachment	10 (23.8)	9 (15.5)	0.31
Neovascular glaucoma	8 (19.1)	7 (12.1)	0.34
Secondary glaucoma requiring anti-glaucoma medications	2 (4.8)	11 (19)	0.02*
Disk pallor	32 (76.2)	41 (70.5)	0.54
Cataract requiring surgery	17 (40.5)	35 (60.3)	0.05*
Tamponade agent used			
Silicone oil	36 (85.7)	51 (87.9)	0.75
Air	4 (9.5)	5 (8.6)	0.87
SF6 gas	2 (4.8)	2 (3.4)	0.75

*P<0.05 statistically significant

Table 3: Visual outcomes based on the type of preoperative diagnosis in the T1DM and T2DM groups

Type of Detachment	T1DM group				T2DM group			
	Eyes	Pre-VA Median (IQR)	Final VA Median (IQR)	P	Number of Eyes	Pre-VA Median (IQR)	Final VA Median (IQR)	P
Dense VH with fibrovascular proliferation	11	1.47 (1.24-1.62)	0.6 (0.39-0.88)	0.05*	18	1.39 (1.20-1.77)	0.47 (0.47-0.77)	0.0001*
Extramacular TRD	6	1.42 (1.02-2.17)	1.07 (0.84-2.29)	0.45	12	1.30 (1.23-1.90)	0.68 (0.47-1.11)	0.01*
Macular TRD	21	1.30 (1.07-1.77)	1.07 (0.77-2.40)	0.37	21	1.47 (1.30-1.77)	1.07 (0.77-2.10)	0.17
CRD	4	2.04 (1.65-2.40)	0.6 (0.6-0.77)	0.01*	7	1.77 (1.77-2.30)	0.77 (0.77-1.00)	0.0001*

VH - vitreous hemorrhage, TRD - tractional retinal detachment, CRD - combined tractional rhegmatogenous detachment. *P<0.05 statistically significant

PDR patients. In our study, preoperative IVB was used in only 16.7% of the cases in the T1DM group and was reserved for cases with florid neovascular membranes with anticipated heavy intraoperative bleeding. A low incidence of POVH in our study suggests that meticulous intraoperative hemostasis by using valved cannulas, immediate and adequate diathermy of bleeders, and raising the bottle height to 60 or 80 mm of Hg largely obviates the need for pre-op IVB except in select cases. Also, patients injected with an anti-vascular endothelial growth factor (VEGF) need to be operated on by 5–7 days, else aggravated TRD may happen, which can make the visual outcome guarded. This is especially important when patients

delay surgery after taking an intravitreal injection, which may be due to the poor socioeconomic status and less awareness regarding the complications of PDR. With 50% of the T1DM patients in our series being hypertensive and 42.85% having CKD, which itself could be a contraindication for anti-VEGF, we have minimized the use of anti-VEGF agents to the cases with highly vascular membranes.

The previous studies have shown cataract progression to be more common in diabetic patients,^[23] and in our study also, 40.5% of the eyes in the T1DM group and 60.3% of the eyes in the T2DM group had progression of cataract post-vitrectomy. Liao *et al.*^[12] found postoperative nuclear sclerosis to be one

of the most common complications after vitrectomy in young diabetic patients (53.4%) during their 2-year follow-up period.

To identify the factors associated with poor visual outcome in both the groups, linear regression analysis was performed [Table 4], which showed that preoperative macular TRD and neovascular glaucoma in both the groups, CKD and lack of preoperative PRP in the T1DM group, HTN, and resurgery in the T2DM group were risk factors for poor visual outcome at the final follow-up. The pre-existing traction detachment of the macula has been observed to be a poor prognostic indicator and the functional outcomes often lag behind anatomic attachment outcomes.^[24] The dissection of FVP by the delamination technique in a detached macula is a complex task requiring appropriate identification of the tissue planes, which if not done meticulously can lead to breaks with unrelieved traction ultimately jeopardizing the outcomes in these eyes. The eyes with MTRD did not achieve statistically significant improvement in both the groups as shown in Table 3. Nephropathy is a microvascular complication similar to retinopathy extensively affecting the microcirculation of the retina and in advanced PDR may result in the progression of FVP and ultimately poor prognosis after surgery.^[10,19] Indeed, out of the 14 eyes of 14 patients with BCVA \leq 20/400 in the T1DM group, DN was present in 7 patients. Lin *et al.*^[25] in their study suggested that surgery on an eye with extensively damaged microcirculation, as in the patients with poor renal function, would lead to poor visual outcomes. Studies have shown that the severity of DR is related to the level of intravitreal VEGF and inflammatory cytokines such as IL-6, which increase due to retinal ischemia, thereby, leading to DR progression.^[26] It has

also been suggested that PRP might prevent this advancement of DR. In our study, 54.5% of the patients in the T1DM who did not undergo preoperative PRP ended up with PL or No PL vision at the final follow-up in comparison to 9.7% of the patients who underwent PRP in the same group. Younger age is a significant risk factor for postoperative NVG and the presence of NVG has been associated with worse visual outcomes^[11] Out of the 8 eyes with NVG in the T1DM group, 6 eyes (75%) had PL or No PL vision at the final follow-up, as against 57.14% of the patients with NVG in the T2DM group who had the same finding. Systemic hypertension affects DR by both hemodynamic (impaired autoregulation and hyperperfusion) and VEGF-induced mechanisms. The VEGF levels are upregulated in the retinal endothelial cells and ocular fluids in the eyes with hypertension.^[27] Nishi *et al.*^[28] found an association between the systemic risk factors and visual acuity at 2 and 4 years following vitrectomy for PDR which is similar to our findings of the association between hypertension and the final visual outcome in the T2DM group.

The strengths of this study include the substantial proportion of eyes with complex PDR in young diabetic patients, both type 1 and type 2, operated on by experienced surgeons with similar techniques at a single institution. Distinguishing T1DM in adult-onset diabetes is challenging and these patients may be erroneously classified with certain forms of type 2 diabetes. The limitations of this study were lack of clinical data like BMI (body mass index), lipid profile, preoperative description of PVD status, intraoperative retinal break descriptions, and lack of standardization regarding the use of preoperative IVB

Table 4: The coefficient and P in the linear regression test for probable risk factors of poor visual prognosis in the T1DM and T2DM groups

Parameter	Type 1 DM		Type 2 DM	
	Coefficient	P	Coefficient	P
Age at surgery	0.005	0.970	-0.141	0.111
Diagnosis at surgery	-0.023	0.857	0.043	0.637
HbA1c	-0.035	0.800	0.088	0.358
Systolic blood pressure	-0.064	0.620	-0.050	0.601
Diastolic blood pressure	-0.051	0.678	0.045	0.617
Serum creatinine	-0.039	0.786	-0.041	0.651
History of cardiovascular disease	0.102	0.388	-0.018	0.841
Chronic kidney disease	0.499	0.028*	0.063	0.486
Duration of diabetes	0.042	0.737	-0.153	0.087
Male gender	0.079	0.507	-0.021	0.822
Recurrent retinal detachment	0.202	0.078	-0.016	0.891
Post-op vitreous hemorrhage	-0.066	0.634	-0.172	0.130
Secondary glaucoma	0.023	0.843	-0.096	0.315
Optic atrophy	0.146	0.239	0.048	0.621
Cataract surgery	0.221	0.057	0.076	0.396
Pre-op PRP	-0.504	0.049*	0.056	0.539
Pre-op IVB	0.016	0.896	0.019	0.856
Neovascular glaucoma	0.1208	0.000*	1.42	0.00*
Resurgery	0.087	0.470	0.433	0.00*
Presence of systemic hypertension	-0.015	0.913	0.377	0.008*
Macular tractional retinal detachment (MTRD)	0.728	0.002*	0.293	0.030*

*P<0.05 statistically significant

and tamponade agent, which were left to the surgeon's discretion and complexity of the membrane dissection involved. The limited sample size and the retrospective nature of the study with all its inherent biases could also be deemed to be a drawback in suggesting causal associations. Larger prospective studies would allow for a more accurate comparison between the two groups and provide further insights on the outcomes following diabetic vitrectomy in the younger population.

Conclusion

In conclusion, the final visual outcomes and anatomic attachment rates post-vitrectomy were poorer in the T1DM group as compared to the T2DM group. Preoperative MTRD and NVG in both groups limited the visual gains. Systemic comorbidities like CKD were more prevalent in the T1DM group and also contributed to the adverse outcomes. Given the limited literature regarding the outcomes of diabetic vitrectomy in the T1DM group, all efforts need to be made to prevent debilitating, sight-threatening complications of T1DM like TRD by highlighting the importance of metabolic control during patient counseling which would improve the outcomes in these patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Katulanda P, Waniganayake YC, Ranasinghe P, Wijetunga WU, Jayaweera M, Wijesinghe NP, *et al.* Retinopathy among young adults with diabetes mellitus from a tertiary care setting in Sri Lanka. *BMC Endocr Disord* 2014;14:20.
- Rajalakshmi R, Rani CS, Venkatesan U, Unnikrishnan R, Anjana RM, Rani SJ, *et al.* Correlation between markers of renal function and sight-threatening diabetic retinopathy in type 2 diabetes: A longitudinal study in an Indian clinic population. *BMJ Open Diabetes Res Care* 2020;8:e001325.
- Laiginhas R, Madeira C, Lopes M, Neves JS, Barbosa M, Rosas V, *et al.* Risk factors for prevalent diabetic retinopathy and proliferative diabetic retinopathy in type 1 diabetes. *Endocrine* 2019;66:201-9.
- Das AK. Type 1 diabetes in India: Overall insights. *Indian J Endocrinol Metab* 2015;19(Suppl 1):S31-3.
- International Diabetes Federation. *IDF Diabetes Atlas*. 8th ed. Brussels, Belgium. Available from: <http://www.diabetesatlas.org>.
- Rajalakshmi R, Amutha A, Ranjani H, Ali MK, Unnikrishnan R, Anjana RM, *et al.* Prevalence and risk factors for diabetic retinopathy in Asian Indians with young onset type 1 and type 2 diabetes. *J Diabetes Complications* 2014;28:291-7.
- Stewart MW, Browning DJ, Landers MB. Current management of diabetic tractional retinal detachments. *Indian J Ophthalmol* 2018;66:1751-62.
- Wong J, Molyneaux L, Constantino M, Twigg SM, Yue DK. Timing is everything: Age of onset influences long-term retinopathy risk in type 2 diabetes, independent of traditional risk factors. *Diabetes Care* 2008;31:1985-90.
- Storey PP, Ter-Zakarian A, Philander SA, De Koo LO, George M, Humayun MS, *et al.* Visual and anatomical outcomes after diabetic traction and traction-rhegmatogenous retinal detachment repair. *Retina* 2018;38:1913-19.
- Huang CH, Hsieh YT, Yang CM. Vitrectomy for complications of proliferative diabetic retinopathy in young adults: Clinical features and surgical outcomes. *Graefes Arch Clin Exp Ophthalmol* 2017;255:863-71.
- Chen HJ, Wang CG, Dou HL, Feng XF, Xu YM, Ma ZZ. Effect of intravitreal ranibizumab pretreatment on vitrectomy in young patients with proliferative diabetic retinopathy. *Ann Palliat Med* 2020;9:82-9.
- Liao M, Wang X, Yu J, Meng X, Liu Y, Dong X, *et al.* Characteristics and outcomes of vitrectomy for proliferative diabetic retinopathy in young versus senior patients. *BMC Ophthalmol* 2020;20:416.
- Shroff CM, Gupta C, Shroff D, Atri N, Gupta P, Dutta R. Bimanual microincision vitreous surgery for severe proliferative diabetic retinopathy: Outcome in more than 300 eyes. *Retina* 2018;38(Suppl 1):S134-45.
- Sokol JT, Schechet SA, Rosen DT, Ferenchak K, Dawood S, Skondra D. Outcomes of vitrectomy for diabetic tractional retinal detachment in Chicago's county health system. *PLoS One* 2019;14:e0220726.
- Choovuthayakorn J, Khunsongkiet P, Patikulsilpa D, Watanachai N, Kunavisarut P, Chaikitmongkol V, *et al.* Characteristics and outcomes of pars plana vitrectomy for proliferative diabetic retinopathy patients in a limited resource tertiary center over an eight-year period. *J Ophthalmol* 2019. doi: 10.1155/2019/9481902.
- Ostri C, la Cour M, Lund-Andersen H. Diabetic vitrectomy in a large type 1 diabetes patient population: Long-term incidence and risk factors. *Acta Ophthalmol* 2014;92:439-43.
- Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, *et al.* Retinopathy in diabetes. *Diabetes Care* 2004;27(Suppl 1):s84-7.
- Batchelder T, Barricks M. The Wisconsin epidemiologic study of diabetic retinopathy. *Arch Ophthalmol* 1995;113:702-3.
- Wu YB, Wang CG, Xu LX, Chen C, Zhou XB, Su GF. Analysis of risk factors for progressive fibrovascular proliferation in proliferative diabetic retinopathy. *Int Ophthalmol* 2020;40:2495-502.
- Eppens MC, Craig ME, Cusumano J, Hing S, Chan AKF, Howard NJ, *et al.* Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. *Diabetes Care* 2006;29:1300-6.
- Michalewska Z, Bednarski M, Michalewski J, Jerzy N. The role of ILM peeling in vitreous surgery for proliferative diabetic retinopathy complications. *Ophthalmic Surg Lasers Imaging Retina* 2013;44:238-42.
- Rush RB, Del Valle Penella A, Reinauer RM, Rush SW, Bastar PG. Internal limiting membrane peeling during vitrectomy for diabetic vitreous hemorrhage: A randomized clinical trial. *Retina* 2021;41:1118-26.
- Klein BE, Klein R, Moss SE. Incidence of cataract surgery in the Wisconsin epidemiologic study of diabetic retinopathy. *Am J Ophthalmol* 1995;119:295-300.
- Yorston D, Wickham L, Benson S, Bunce C, Sheard R, Charteris D. Predictive clinical features and outcomes of vitrectomy for proliferative diabetic retinopathy. *Br J Ophthalmol* 2008;92:365-8.
- Lin SJ, Yeh PT, Huang JY, Yang CM. Preoperative prognostic factors in vitrectomy for severe proliferative diabetic retinopathy. *Taiwan J Ophthalmol* 2014;4:174-8.
- Suzuki Y, Adachi K, Maeda N, Tanabu R, Kudo T, Nakazawa M. Proliferative diabetic retinopathy without preoperative pan-retinal photocoagulation is associated with higher levels of intravitreal IL-6 and postoperative inflammation. *Int J Retina Vitreous* 2020;6:24.
- Srivastava BK, Ramya B, Prathiba V, Mohan V. Systemic factors affecting diabetic retinopathy. *J Diabetology* 2018;9:73-7.
- Nishi K, Nishitsuka K, Yamamoto T, Yamashita H. Factors correlated with visual outcomes at two and four years after vitreous surgery for proliferative diabetic retinopathy. *PLoS One* 2021;16:e0244281.