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Clinical Profile and Ocular Morbidities in Patients with Both Diabetic Retinopathy and Uveitis

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Purpose: To describe the clinical profile and complications of diabetic retinopathy (DR) and uveitis in patients with coexisting conditions and to derive associations based on site of primary inflammation, stage of DR, and complications of each.

Design: Single-center, cross-sectional observational study.

Participants: Sixty-six patients with coexisting DR and uveitis.

Methods: Electronic medical records of 66 such cases were evaluated. The demographic data, diabetic status, clinical characteristics, and complications of DR and uveitis on the final follow-up were recorded.

Main Outcome Measures: Associations between best corrected visual acuity (BCVA), prevalence of various stages, and complications of DR among eyes with and without uveitis, and correlation between the intensity and primary sites of inflammation among eyes with proliferative and nonproliferative changes.

Results: Of the 132 eyes, all had DR and 97 eyes had uveitis (35 unilateral and 31 bilateral cases). Mean age of patients was 53.4 ± 8.7 years, duration of diabetes was 10.5 ± 6.9 years, and duration of uveitis was 61.3 ± 68.8 months. Of uveitis patients, 54.6% had anterior uveitis (AU), 20.6% had intermediate, 10.3% posterior, and 14.4% panuveitis. Forty-nine point five percent of eyes had proliferative DR (PDR) changes. There was a higher proportion PDR cases among anterior (56.6%), posterior (70%), and panuveitis (64.3%), with difference in AU cases approaching statistical significance ($P = 0.067$). Conversely, significant ($P < 0.001$) intermediate uveitis cases had nonproliferative changes (80%). Final BCVA was significantly poorer in the group with uveitis ($P = 0.045$). The proportion of fibrovascular proliferations, tractional detachments. and iris neovascularization among proliferative retinopathy eyes with uveitis (14.6%, 18.8%, and 12.5% respectively) was higher than those without uveitis (5.3%, 10.5%, and 5.3%). Among uveitis cases, 58.5% eyes developed cataracts, 44.3% had posterior synechiae, 12.3% developed secondary glaucoma, 4.1% had epiretinal membrane, 4.1% had band-shaped keratopathy, and 1.0% developed macular neovascularization.

Conclusions: Eyes with coexisting DR and uveitis have a higher prevalence of neovascular and uveitis complications along with a risk of poorer visual outcomes. Treatment should aim at limiting the duration and intensity of inflammation. Strict glycemic control is essential for inflammation control and preventing the progression of DR to more advanced stages.

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Diabetic retinopathy (DR) is a common microvascular complication of long-term diabetes mellitus (DM). The annual incidence of DR ranges from 2.2% to 12.7%, whereas the annual incidence of proliferative disease ranges from 0.03% to 0.72%.[1] Uveitis, on the other hand, is a group of inflammatory disorders of the uveal tract with an annual incidence of 17 to 52 per 100 000 people but affects younger people.[2] Both uveitis and DR are vision-threatening conditions that can have disastrous consequences when they coexist.

There have been conflicting reports in the literature regarding the effect of uveitis on DR status.[3–6] Similar to DR, uveitis results in a breakdown of blood-retinal-barrier and increased accumulation of proinflammatory factors (interleukin 6 and 8 and tumor necrosis factor-α) and VEGF.[6] These common pathophysiological mechanisms can further augment the process of DR progression. Similarly, vasculitis-induced ischemia in uveitis is known to exacerbate the preexisting hypoxia in DR and worsen the DR.[7] And complications of uveitis, such as secondary glaucoma, optic atrophy, and extensive chorio-retinal atrophy, may reduce the metabolic demand of the retinal tissue and impede DR progression.[7,8]

Diabetes mellitus can also affect the course and outcome of uveitis in the eyes. Preexisting diabetes is associated with an exaggerated inflammatory response during uveitic

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episodes, resulting in a higher degree of complications.[9] Poor glycemic control, which is frequently caused by the side effects of systemic corticosteroids used to treat uveitis, can be linked to more severe inflammation.[10] Despite the well-documented pathophysiological mechanisms, there have been very few studies describing the clinical characteristics of eyes with coexisting DR and uveitis. The purpose of this study is to describe the clinical profile and complications of DR and uveitis in eyes with concurrent conditions, as well as to evaluate associations based on the site of primary inflammation, DR grade, and complications of each.

Methods

A cross-sectional observational study was conducted on all patients with DM who presented to a tertiary care center in South India and were diagnosed with DR and uveitis. Clinical records of patients were reviewed. The study was carried out in accordance with the ethical standards established in the Declaration of Helsinki and according to the guidelines of the local institutional review board. Baseline data were collected on their age, gender, age of onset and duration of diabetes, type of diabetes, current diabetes treatment, and degree of control. The Indian Council of Medical Research guidelines-2018 were used to classify diabetes control, with satisfactory control ("controlled") defined as fasting blood sugar 125 mg/dl, postprandial blood sugar $\leq$ 180 mg/dl, and glycosylated hemoglobin $<$ 8. Unsatisfactory control was defined as any values that exceeded these cut-off criteria ("uncontrolled"). Diabetes comorbidities and end-organ sequelae were also documented.

The final visit examination data were collected. It included best corrected visual acuity (BCVA) using Snellen's visual acuity chart, intraocular pressure measured using Goldmann applanation tonometry, uveitis subtypes based on the Standardization of Uveitis Nomenclature criteria, Standardization of Uveitis Nomenclature grading of peak inflammation (cells and flare), and complications associated with uveitis. The inflammation was graded based on the peak uveitis episode. The duration of the uveitis and the number of recurrences were also recorded.

For DR, the final DR grading was recorded using the modified Early Treatment DR classification (mild, moderate, severe nonproliferative DR [NPDR], proliferative DR [PDR], and advanced diabetic eye disease [ADED]), and the complications associated with DR were noted. Advanced diabetic eye disease (based on Early Treatment DR classification) included eyes with preretinal or intragel hemorrhage, tractional retinal detachment, or rubeosis iridis.

Differential statistics were used to compute the mean, range, and standard deviation. Inferential statistics were performed using the chi-square test and the independent *t* test in MedCalc 20.115, with a *P* value of $\leq$ 0.05 considered statistically significant.

Results

The index study included 66 patients who were diagnosed to have DR and uveitis simultaneously. Among 132 eyes of these 66 patients with DR, 97 (73.5%) eyes had uveitis. Thirty-eight (57.6%) patients were males, and 28 (42.4%) were females. The mean age (mean $\pm$ standard deviation) at presentation was 53.4 $\pm$ 8.7 years (range: 30-79 years). The mean duration of diabetes was 10.5 $\pm$ 6.9 years (range: 0-25 years). The mean duration of uveitis was 61.3 $\pm$ 68.8 months, and the mean number of recurrences was 2.93 (Table 1). Twenty-five (37.9%) patients had controlled diabetes when they were diagnosed with uveitis, whereas 41 (62.1%) had uncontrolled DM.

All 66 patients were diagnosed with type 2 DM, and there were no patients with type 1 DM in this study.

Table 1. Baseline Characteristics of the Study Subjects

Diabetes Related	
Parameter	*Number of Patients (%)*
Age of onset (yrs)	42.9 $\pm$ 8.7 (mean $\pm$ SD)
Duration (yrs)	10.5 $\pm$ 6.9
Diabetes control	
Controlled	25 (37.9%)
Uncontrolled	41 (62.1%)
Diabetes treatment	
Diet + lifestyle	3 (4.5%)
OHA	35 (53.0%)
OHA + insulin	24 (36.4%)
Insulin	3 (4.5%)
None	1 (1.5%)
DR staging for patients (worse eye)	
Mild NPDR	7 (10.6%)
Moderate NPDR	14 (21.2%)
Severe NPDR	3 (4.5%)
PDR	21 (31.8%)
ADED	21 (31.8%)
Diabetic sequelae	
Nephropathy	10 (15.2%)
Neuropathy	3 (4.5%)
Peripheral gangrene	1 (1.5%)
Comorbidities	
Hypertension	26 (39.4%)
Hypercholesterolemia	12 (18.2%)
CKD	5 (7.6%)
IHD	3 (4.5%)
Uveitis Related	
Parameter	*Number of Eyes (%)*
Uveitic eyes	97 (73.5)
Laterality	
Unilateral	35 (36.1)
Bilateral	62 (63.9)
Duration of uveitis (mos)	61.3 $\pm$ 68.8
Mean no. of episodes	2.93
SUN classification	
Anterior	53 (54.6)
Intermediate	20 (20.6)
Posterior	10 (10.3)
Panuveitis	14 (14.4)
SUN grading of cells	
0	22 (22.7)
0.5+	15 (15.5)
1+	27 (27.8)
2+	28 (28.9)
3+	5 (5.2)
4+	0

ADED = advanced diabetic eye disease; CKD = chronic kidney disease; DR = diabetic retinopathy; IHD = ischemic heart disease; NPDR = nonproliferative diabetic retinopathy; OHA = oral hypoglycemic agents, PDR = proliferative diabetic retinopathy; SD = standard deviation; SUN = Standardization of Uveitis Nomenclature.

Diabetic treatment comprised of dietary regulation in 3 patients, oral hypoglycaemic agents in 35 patients, a combination of oral hypoglycaemic agents and insulin in 24 patients, and only insulin in 3 patients. One patient was not on any treatment on presentation with uveitis. On presentation, 10 patients had coexistent diabetic nephropathy and 5 of them had progressed to chronic kidney disease.

Ten patients (15.2%) had developed diabetic nephropathy, 3 (4.5%) had diabetic neuropathy, and 1 patient (1.5%) had a history of right forefinger amputation following gangrene. The associated comorbidities included 26 patients with hypertension, 12 with hypercholesterolemia, 5 with systemic tuberculosis (TB), 3 with ischemic heart disease, and 3 patients with a history of stroke. On the final follow-up, 7 patients (10.6%) had mild NPDR, 14 (21.2%) had moderate NPDR, 3 (4.5%) had severe NPDR, 21 (31.8%) had PDR, and 21 (31.8%) had ADED in the worse eye (Table 1).

Among the uveitic eyes (n = 97), 35 patients had unilateral uveitis, whereas 31 patients (62 eyes) had bilateral uveitis. The most common subtype of uveitis in these patients was anterior uveitis (AU) eyes in 53 cases (54.6%), followed by intermediate uveitis in 20 eyes (20.6%), posterior in 10 (10.3%), and panuveitis in 14 eyes (14.4%) (Table 1).

The etiology of uveitis was determined in 31 (47.0%) cases. Among the noninfectious causes, 27 cases (40.9%) were categorized as idiopathic AU, followed by 8 cases of sarcoidosis associated uveitis (12.1%), and 6 idiopathic intermediate uveitis (9.1%). Among the infectious causes, the most common etiology was TB associated uveitis (10.6%), followed by 2 cases of herpes simplex virus associated AU (3.0%), and 1 case of toxoplasma retino-choroiditis (1.5%). The etiological classifications of uveitis have been described in Table 2.

Twenty-five of the patients were started on oral steroids for the treatment of uveitis, and 8 patients were on immunesuppressives (4 on Azathioprine, 2 on Methotrexate, 1 on mycophenolate mofetil, and 1 patient on cyclosporine). Seven patients additionally received anti-TB therapy for ocular TB, and 2 patients were started on oral acyclovir for herpetic kerato-uveitis. Thirteen eyes received sub-tenon steroid injection and 3 eyes received intravitreal triamcinolone acetonide for the inflammation.

Table 2. Etiological Diagnosis of Uveitis

Diagnosis	N (%)
Idiopathic anterior uveitis	27 (40.9%)
Sarcoidosis associated uveitis	8 (12.1%)
TB associated uveitis	7 (10.6%)
Idiopathic intermediate uveitis	6 (9.1%)
Multifocal choroiditis	4 (6.0%)
Rheumatoid arthritis associated AU	3 (4.5%)
HLA B27 associated AU	3 (4.5%)
Idiopathic retinal vasculitis	2 (3.0%)
Sympathetic ophthalmitis	2 (3.0%)
HSV associated AU	2 (3.0%)
Toxoplasma retinochoroiditis	1 (1.5%)
SLE associated AU	1 (1.5%)

AU = anterior uveitis; HLA = human leukocyte antigen; HSV = herpes simplex virus; SLE = systemic lupus erythematosus; TB = tuberculosis.

Among the complications, in eyes with uveitis (n = 97), 57 (58.5%) eyes developed cataracts, 43 (44.3%) had posterior synechiae (PS), 12 (12.3%) developed secondary glaucoma, 4 (4.1%) had epiretinal membrane, 4 (4.1%) had band-shaped keratopathy, and 1 (1.0%) developed macular neovascularization. One eye was also noted to have an exudative retinal detachment. Among the DR eyes without uveitis, 16 (45.7%) had cataract, 2 (5.7%) had developed glaucoma, and 2 (5.7%) had developed epiretinal membrane. The complications of DR eyes, with and without uveitis, have been mentioned in Table 3.

Among the eyes with uveitis (n = 97), the mean BCVA on final follow-up was 0.98 ± 0.9 in logarithm of the minimum angle of resolution. There were 13 (13.4%) uveitis eyes with mild NPDR, 19 (19.6%) with moderate NPDR, 8 (8.2%) with severe NPDR, 27 (27.8%) with PDR, and 21 (21.6%) with ADED (Table 4). Seven eyes had fibrovascular proliferations (FVP) as DR sequelae, 7 had neovascularization at the disc, 18 had diabetic macular edema (DME), 5 had preretinal hemorrhage, 10 had vitreous hemorrhage, 9 had tractional retinal detachments (TRD), 2 developed neovascular glaucoma, and 6 eyes developed neovascularization of the iris (NVI).

Similarly, among the nonuveitic eyes (35 eyes), the mean BCVA on final follow-up was 0.61 ± 1.0 in logarithm of the minimum angle of resolution. The difference in BCVA among uveitic and nonuveitic eyes was found to be statistically significant ($P = 0.045$). There were 8 (22.9%) nonuveitis eyes with mild NPDR, 4 (11.4%) with moderate NPDR, 3 (8.6%) with severe NPDR, 12 (34.3%) with PDR, and 7 (20%) with ADED (Table 4). One eye had FVP, 3 had neovascularization at the disc, 3 had DME, 3 had preretinal hemorrhage, 4 had vitreous hemorrhage, 2 had TRDs, 1 developed neovascular glaucoma, and 1 eye developed NVI.

The anatomical location of the inflammation has been categorized among proliferative and NPDR eyes in Table 5. Among the cohort of eyes with uveitis (n = 97), 18 (33.9%) of the eyes with AU had NPDR, whereas 30 (56.6%) had PDR changes. This difference almost reached statistical significance ($P = 0.068$). Sixteen (80%) eyes with intermediate uveitis had NPDR, and only 2 (10%) eyes had PDR changes, reaching a statistically significant value ($P < 0.001$). Of eyes with posterior uveitis, 30% had NPDR, and 70% had PDR changes ($P = 0.305$). Of eyes with panuveitis, 21.4% had NPDR, and 64.3% had PDR ($P = 0.128$).

Table 6 illustrates the vascular complications noted among all uveitic and nonuveitic eyes with PDR (n = 67). The proportion of FVP, TRD, and NVI among PDR eyes with uveitis (14.6%, 18.8%, and 12.5%, respectively) was noted to be higher than that of nonuveitic PDR eyes (5.3%, 10.5%, and 5.3%), although the values did not reach statistical significance.

The DR characteristics in both eyes of unilateral uveitis cases (n = 70) are listed in Table 7. The proportion of nonproliferative and proliferative retinopathy eyes among

Table 3. Ocular Complications due to DR and Uveitis

Complications	Prevalence in Eyes with Uveitis (n = 97)	Prevalence in DR Eyes without Uveitis (n = 35)	P Value
Cataract	57 (58.8)	16 (45.7%)	0.183
Posterior synechiae	43 (44.3)	0 (0%)	-
DME	18 (18.6%)	3 (8.6%)	0.168
Glaucoma	12 (12.3%)	2 (5.7%)	0.278
VH	10 (10.3%)	4 (11.4%)	0.857
TRD	9 (9.3%)	2 (5.7%)	0.511
FVP	7 (7.2%)	1 (2.9%)	0.363
NVD	7 (7.2%)	3 (8.6%)	0.789
NVI	6 (6.2%)	1 (2.9%)	0.458
PRH	5 (5.2%)	3 (8.6%)	0.473
ERM	4 (4.1%)	2 (5.7%)	0.697
BSK	4 (4.1%)	0 (0%)	-
Hypopyon	3 (3.1%)	0 (0%)	-
NVG	2 (2.1%)	1 (2.9%)	0.788
MNV	1 (1.0%)	0 (0%)	-

BSK = band shaped keratopathy; DME = diabetic macular edema; DR = diabetic retinopathy; ERM = epiretinal membrane; FVP = fibrovascular proliferation; MNV = macular neovascularization; NVD = neovascularization of disc; NVG = neovascular glaucoma; NVI = neovascularization of iris; PRH = preretinal hemorrhage; TRD = tractional retinal detachment; VH = vitreous hemorrhage.

eyes with uveitis were 31.4% and 54.3%, respectively, and that among nonuveitic eyes was 40% and 51.4%, respectively. The proportion of eyes with DME, vitreous hemorrhage, and TRD was higher among uveitic eyes (14.3%, 14.3%, and 8.6%) than nonuveitic eyes of unilateral cases (8.6%, 11.4%, and 5.7%), though the values did not attain statistical significance.

Discussion

The purpose of this cross-sectional study was to characterize the manifestations of DR and uveitis in the sample population and to establish relevant associations. To the best of our knowledge, this is the largest cohort of patients with coexisting DR and uveitis in which the prevalence, clinical profile, and sequelae of both conditions have been described. We found a higher prevalence of uveitis (cataract and PS) and DR complications (DME, FVP, TRD, and NVI) than previously reported in eyes with isolated conditions.[11–14] The BCVA was significantly higher in eyes with isolated DR than in eyes with DR and uveitis. Non-PDR was found to be significantly more prevalent in eyes with intermediate uveitis than PDR. However, among the other uveitis types (anterior, posterior, and panuveitis), PDR was found to be the most common DR stage. The latter values did not reach statistical significance.

Table 4. DR Staging in Eyes with and without Uveitis

	Eyes with Uveitis (n = 97)	Eyes without Uveitis (n = 35)	P Value
BCVA at final visit	0.98 ± 0.9	0.61 ± 1.0	0.045*
Pseudophakic	21 (21.65%)	7 (20%)	
Cataractous	57 (58.76%)	16 (45.71%)	
Clear lens	19 (19.59%)	12 (34.29%)	
DR staging			
Mild NPDR	13 (13.4%)	8 (22.9%)	0.191
Moderate NPDR	19 (19.6%)	4 (11.4%)	0.277
Severe NPDR	8 (8.2%)	3 (8.6%)	0.953
PDR	27 (27.8%)	12 (34.3%)	0.475
ADED	21 (21.6%)	7 (20%)	0.839
Cannot assess	9 (9.3%)	1 (2.9%)	

ADED = advanced diabetic eye disease; BCVA = best corrected visual acuity; DR = diabetic retinopathy; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.
*Statistically significant.

Our study group had a much higher prevalence of PDR eyes (49.5%) than the general population.[15] Several case reports in the literature have substantiated the rapid progression of DR in eyes with uveitis.[3,6,9] Pathophysiological mechanisms in uveitis, such as blood-retinal-barrier breakdown and VEGF accumulation, have been shown to worsen DR progression.[6] Poor glycemic control, a known risk factor for uveitis in diabetic patients, also influences DR status.[10,13] Similarly, in our cohort, we found a higher proportion of eyes with PDR changes among the anterior (56.6%), posterior (70%), and panuveitis cases (64.3%). The difference in cases of AU approached statistical significance ($P = 0.067$).

However, among the intermediate uveitis cases, we found a significantly higher proportion of NPDR eyes (80%) than PDR (10%), with the difference being statistically significant. This could be explained by the fact that our PDR diagnosis was based primarily on the presence of neovessels with accompanying ischemic retina. Few peripheral neovascularization-elsewhere in uveitis eyes were classified as a result of inflammation rather than PDR. Furthermore, intermediate uveitis has been linked to an earlier onset of posterior vitreous detachment, which prevents the further progression of DR into proliferative stages.[16] In view of the very small sample size of eyes with intermediate uveitis without neovascularization elsewhere (n = 2) in our study, we could not provide a detailed analysis and reliable

Table 5. SUN Classification of Uveitis in Proliferative and Nonproliferative DR

	Nonproliferative DR (n = 40)	Proliferative DR (n = 48)	Not Assessed	*P* Value
SUN classification				
Anterior	18 (45)	30 (64.6)	5	0.067*
Intermediate	16 (40)	2 (4.2)	2	< 0.0001*
Posterior	3 (7.5)	7 (14.6)	0	0.305
Pan	3 (7.5)	9 (18.8)	2	0.128
SUN grading of cells at presentation				
0	8 (21.0)	12 (24)	2	0.745
0.5+	4 (10.5)	9 (18)	2	0.331
1+	12 (31.6)	13 (26)	2	0.568
2+	12 (31.6)	13 (26)	3	0.568
3+	2 (5.3)	3 (6)	0	0.883

DR = diabetic retinopathy; SUN = Standardization of Uveitis Nomenclature.
*Statistically significant.

exposition regarding the effect of other contributing factors in this statistical significance. This would need further exploration.

Prieto Del Cura MDM et al[11] discovered a 20.8% prevalence of cataract and a 28.7% prevalence of PS in his uveitis patient cohort. In contrast, Oswal et al[9] demonstrated a prevalence of 37.9% cataract and 50% PS in his diabetic and uveitis patients, which was more comparable to our values. Because the average age of the patients in all 3 studies was comparable, the difference can be attributed to the more intense inflammation seen in diabetics during uveitic episodes.[10] This contributes to a higher prevalence of complications. Furthermore, diabetics have a higher prevalence of cataract than the general population at their age. The incidence of cataract was found to be only slightly higher in DR patients than in the general diabetic population.[12] Although the difference was not statistically significant, the prevalence of neovascular complications (FVP, TRD, and NVI) in PDR eyes was found to be higher in uveitis eyes than in nonuveitis eyes with PDR. In contrast to DR, where retinal ischemia is the primary cause of neovascular changes, uveitic neovascularization is primarily due to chronic inflammation.[17] According to Arevalo et al,[18] TRDs are present in 1.5% of uveitic eyes. In these cases, he proposed neovascularization elsewhere followed by gliosis as the most common pathology. Jalil et al,[19] on the other hand, proposed a tractional pathogenesis for the occurrence of peripheral TRDs and FVPs in intermediate uveitis eyes. Similarly, Lightman et al and Vela et al independently found TRDs in 2 cases of healed candida chorioretinitis, which they attributed to contraction of inflammatory epiretinal fibroproliferative membranes.[20,21] All this could contribute to the development of TRDs in our cohort. As a result, the additive effect of uveitis sequelae, as well as the higher incidence of DR complications in the combination eyes, explains the statistically significant visual acuity difference observed when compared with eyes with DR changes alone. In contrast to previous studies, our cohort had a much lower prevalence of severe inflammation (> 2+) on the first presentation with uveitis.[9,10,22,23]

Table 6. Vascular Complications Among PDR Cases with and without Uveitis

Complications	PDR Eyes with Uveitis (n = 48)	PDR Eyes without Uveitis (n = 19)	*P* Value
FVP	7 (14.6%)	1 (5.3%)	0.293
NVD	7 (14.6%)	3 (15.8%)	0.522
PRH	5 (10.4%)	3 (15.8%)	0.541
VH	10 (20.9%)	4 (21.1%)	0.984
TRD	9 (18.8%)	2 (10.5%)	0.416
NVG	2 (4.2%)	1 (5.3%)	0.846
NVI	6 (12.5%)	1 (5.3%)	0.286

FVP = fibrovascular proliferation; NVD = neovascularization of disc; NVG = neovascular glaucoma; NVI = neovascularization of iris; PDR = proliferative diabetic retinopathy; PRH = preretinal hemorrhage; TRD = tractional retinal detachment; VH = vitreous hemorrhage.

Because our study was conducted in a tertiary care hospital, the inconsistent findings could be attributed to many referred cases who received initial treatment elsewhere. We also found no link between uncontrolled DM and the severity of inflammation, as previously demonstrated.[9,22,23] On presentation with uveitis, however, 62.1% of our patients were found to have uncontrolled diabetes. In the active phase of uveitis, Oswal et al[9] found a significantly higher proportion of patients with glycosylated hemoglobin values > 6.2% than in the quiescent phase. The proportional distribution of uveitis types (anterior, intermediate, posterior, and panuveitis) observed in our study was comparable to that seen in the general population and diabetics.[9,24] As a result, according to our findings, there was no change in the anatomical distribution of inflammation in uveitis among DR eyes.

Our study's strength is the large sample size of patients with coexisting DR and uveitis—one of the largest cohorts

Table 7. DR Characteristics Among Unilateral Uveitis Cases in Eyes with and without Uveitis

	Unilateral Uveitis Cases in Eye with Uveitis (n = 35)	Unilateral Uveitis Cases in Eye without Uveitis (n = 35)	*P* Value
DR Staging			
Mild NPDR	5 (14.3%)	8 (22.9%)	0.360
Moderate NPDR	3 (8.6%)	3 (8.6%)	1.000
Severe NPDR	3 (8.6%)	3 (8.6%)	1.000
PDR	9 (25.7%)	12 (34.3%)	0.436
ADED	10 (28.6%)	6 (17.1%)	0.255
Not assessed	5 (14.3%)	3 (8.6%)	
Vascular complications			
DME	5 (14.3%)	3 (8.6%)	0.455
PRH	2 (5.7%)	2 (5.7%)	1.000
VH	5 (14.3%)	4 (11.4%)	0.723
TRD	3 (8.6%)	2 (5.7%)	1.000
NVD	2 (5.7%)	3 (8.6%)	0.645
NVI	1 (2.9%)	1 (2.9%)	1.000

ADED = advanced diabetic eye disease; DME = diabetic macular edema; DR = diabetic retinopathy; NPDR = nonproliferative diabetic retinopathy; NVD = neovascularization disc; NVI = neovascularization of iris; PDR = proliferative diabetic retinopathy; PRH = preretinal hemorrhage; TRD = tractional retinal detachment; VH = vitreous hemorrhage.

documented in the literature. Only systemic parameters and glycemic status were available for patients to be correlated with uveitis onset and severity. Among the larger cohorts, Patel et al[17] had conducted a large cohort retrospective study among uveitic eyes of 8931 patients to study the prevalence and incidence of neovascularization. Ansari et al,[25] on the other hand, conducted a 6 year study to evaluate the prevalence of uveitis among people without (n = 889 856) and with diabetes (n = 48 584) and demonstrated glycemic control as a modifiable risk factor.

Because of its retrospective nature, our study has the limitations that all retrospective studies have. The control arm was small, consisting of eyes with and without uveitis. Because this was a cross-sectional study, we could not assess the relative risk of DR progression in the presence of uveitis, as well as the long-term implications in these eyes. Furthermore, the fact that the data are gathered from a single institute may result in bias. A prospective multicenter study could provide a more comprehensive understanding of the course and outcomes of eyes with DR and uveitis.

Finally, the development of uveitis in eyes with preexisting DR is associated with significant morbidity and visual consequences. Late-stage DR, neovascular complications, and uveitis sequelae are much more common in these eyes. These patients are also at risk of having poorer visual outcomes. As a result, the therapeutic approach should include an immediate and aggressive strategy to limit the severity and duration of the inflammation. Strict glycemic control is essential for reducing inflammation and preventing the progression of DR to more advanced proliferative stages.

Footnotes and Disclosures

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All authors have completed and submitted the ICMJE disclosures form.

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HUMAN SUBJECTS: Human subjects were included in this study. The study was carried out in accordance with the ethical standards established in the Declaration of Helsinki and according to the guidelines of the local institutional review board.

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Author Contributions:

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Analysis and interpretation: Mohapatra, Raman, Sudharshan, Majumdar, Sreenivasan

Data collection: Mohapatra, Raman, Sudharshan, Majumdar

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Abbreviations and Acronyms:
ADED = advanced diabetic eye disease; **AU** = anterior uveitis; **BCVA** = best corrected visual acuity; **DM** = diabetes mellitus; **DME** = diabetic macular edema; **DR** = diabetic retinopathy; **FVP** = fibrovascular proliferations; **NPDR** = nonproliferative diabetic retinopathy; **NVI** = neovascularization of the iris; **PDR** = proliferative diabetic retinopathy; **PS** = posterior synechiae; **TB** = tuberculosis; **TRD** = tractional retinal detachments.

Keywords:
Diabetic retinopathy, Uveitis, Proliferative diabetic retinopathy.

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