Severity of diabetic retinopathy and its relationship with age at onset of diabetes mellitus in India: A multicentric study

Deepika C Parameswarappa, Ramachandran Rajalakshmi, Ashik Mohamed, Sanagavarapu Kavya, Haripriya Munirathamani, George Manayath, Mathangi Ashok Kumar, Rajeev Raman, TP Vignesh, Kim Ramasamy, Sheena Mani, Alankrita Muralidhar, Manisha Agarwal, Giridhar Anantharaman, Neha Bijlani, Gajendra Chawla, Alok Sen, Sucheta Kulkarni, Umesh C Behera, Sobha Sivaprasad, Taraprasad Das, Padmaja Kumari Rani, on behalf of India Retinal Disease Study group

Purpose: To present clinical profile and risk factors of sight-threatening diabetic retinopathy (STDR) among people with age of onset of diabetes (AOD) <25 versus ≥25 years. Methods: A retrospective chart analysis of consecutive patients with diabetic retinopathy (DR) (n = 654) treated at 14 eye care centers across India between 2018 and 2019 was performed. Patients were divided into two groups, Group 1: AOD <25 years and Group 2: AOD ≥25 years. DR and diabetic macular edema (DME) were classified using the International Clinical Classification of DR severity scale. STDR included severe nonproliferative DR (NPDR), proliferative DR (PDR), and moderate to severe DME. Multilevel mixed-effects model was used for comparison between two groups: 1) Patients with DR and AOD <25 years and 2) Patients with DR and AOD ≥25 years. Bivariate and multivariate regression analyses were used to evaluate risk factors between the two groups.

Results: A total of 654 patients were included, 161 (307 eyes) in AOD <25 and 493 (927 eyes) in AOD ≥25 group. There was a higher prevalence of PDR with high-risk characteristics in AOD <25 group (24% vs. 12%) at baseline and 12-month follow-up (25% vs. 6%); \( P < 0.001 \). Systolic hypertension and poor glycemic control were risk factors in both groups, with no difference in these modifiable risk factors between groups.

Conclusion: People with youth-onset DM are likely to present with severer form of STDR despite similar duration of diabetes in youth as the onset of any type of diabetes in persons less than 25 years of age. In YDR, there are more males, and compared to SEARCH, a higher proportion of individuals had high blood pressure (BP) and poor glycemic control. In the YDR study, an acute diabetes-related complication was 17% with type 1 DM and 42% with type 2 DM. The YDR has

Key words: Age of onset of diabetes, diabetes mellitus, diabetic retinopathy, severity, sight-threatening

Smt Kanuri Santamma Center for Vitreo-Retina Diseases, L V Prasad Eye Institute, Hyderabad, Telangana, 1Department of Ophthalmology, Madras Diabetes Research Foundation and Dr. Mohan’s Diabetes Specialities Centre, Chennai, Tamil Nadu, 2Ophthalmic Biophysics, L V Prasad Eye Institute, Hyderabad, Telangana, 3Aravind Eye Hospital, Coimbatore, Tamil Nadu, 4Sankara Nethralaya, Chennai, Tamil Nadu, 5Aravind Eye Hospital, Madurai, Tamil Nadu, 6Dr. Tony Fernandez Eye Hospital, Aluva, Kerala, 7Dr Shroff’s Charity Eye Hospital, Delhi, 8Giridhar Eye Institute, Kerala, 9Vision Care And Research Centre, Bhopal, Madhya Pradesh, 10Sagdurru Netra Chikitsalaya, Chitrakot, Madhya Pradesh, 11PBMA’s H V Desai Eye Hospital, Pune, Maharashtra, 12Retina Vitreous Service, Mithu Tulsir Charnar campus, L V Prasad Eye Institute, Bhubaneswar, Odisha, India, 13NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, 14Vision Sciences, UCL Institute of Ophthalmology, London, UK

Correspondence to: Dr. Padmaja Kumari Rani, Network Head, Teleophthalmology, L V Prasad Eye Institute, Kallam Anji Reddy Campus, Hyderabad, Telangana - 500 034, India. E-mail: rpk@lvpei.org

Received: 28-May-2021  Revision: 06-Jul-2021
Accepted: 12-Aug-2021  Published: 29-Oct-2021

© 2021 Indian Journal of Ophthalmology | Published by Wolters Kluwer - Medknow
not reported the prevalence of DR youth in India. The rising prevalence in adolescents and young adults is attributed to childhood obesity in the Youth Diabetes Registry (YDR) data of people diagnosed with diabetes under 25 years of age. Unlike the American study where the prevalence of DR in youth was 17%, the YDR has not documented the prevalence of DR in their pediatric cohort. Isolated single-center studies have reported an incidence of 52.9/1000 person years in youth-onset diabetes. 

Apart from strict glycemic control, other factors that significantly influence the severity of DR include age, hypertension, obesity, anemia, nephropathy, neuropathy, cardiopathy, and blood dyscrasias. The prevalence of DR and its association with duration of DM, high systolic BP (SBP), dyslipidemia, diabetic kidney disease, and anemia have been studied in people with T2 DM in India. The burden of systemic risk factors for DR in youth-onset diabetes and older–adult-onset diabetes is not yet studied. The present study aims to compare demographics, clinical features, DR severity, and treatment characteristics between people diagnosed with DM under and after the age of 25 years. The study also aims to evaluate the risk factors associated with sight-threatening diabetic retinopathy (STDR) with respect to the age of onset of DM.

Methods

This is a retrospective, multicenter comparative study across 14 tertiary centers in India. A retrospective review of records of consecutive patients diagnosed with diabetes and DR in the hospital electronic register or case records between January 2018 and December 2019 were collected. Local Institutional Review Boards provided the ethics approval for the study. The study followed the tenets of the Declaration of Helsinki.

Systemic data collected included age at presentation, age of onset of diabetes (AOD), duration of diabetes, duration of hypertension (if present), glycated hemoglobin (HbA1c), and treatment details for DM. Systemic history, AOD, duration of DM, and treatment history were evaluated through medical record files and review of physician records. The collected ocular data included presenting best-corrected Snellen visual acuity, the severity of the DR, DME grade when present, and DR treatment modalities in both eyes. Undilated anterior segment examination was performed. Fundus assessment was performed by slit-lamp biomicroscopy and indirect ophthalmoscopy. Optical coherence tomography (OCT) images were acquired using Heidelberg Spectralis HRA and OCT (Heidelberg Engineering, Heidelberg, Germany), Triton SS-OCT device (Topcon Corporation, Tokyo, Japan), and Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA). The central macular thickness (CMT) was measured manually as the distance between internal limiting membrane and anterior border of RPE-Bruch’s membrane complex at the fovea.

As obtained directly from the OCT, the records with incomplete information were excluded. Baseline data were collected for all patients. Follow-up visits at 3, 6, and 12 months were included, if available. A ±2 months visit window was allowed for each time point.

Patients with DM were stratified into two groups based on the AOD; Group 1: <25 years and Group 2: ≥25 years.

DR and DME were graded according to the International Clinical DR Classification severity scale. PDR with high-risk characteristics (HRC) was defined as the presence of vitreous hemorrhage, new vessels at the disc ≥1/4–1/3 disc area in size, or new vessels elsewhere ≥1/2 disc area in size if associated with vitreous hemorrhage. Patients were also further grouped into STDR and non-STDR (N-STDR) groups. The presence of severe nonproliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR), PDR with HRC, moderate DME, and severe DME were grouped under STDR. The prevalence of mild NPDR, moderate NPDR, and mild DME were grouped under N-STDR. The risk factors for DR were analyzed in both groups. Number of laser sittings, intravitreal injections, and vitreoretinal interventions required in both groups were also analyzed.

The statistical analysis was performed using software STATA v14.2 (StataCorp, College Station, TX, USA). A multilevel mixed-effects model, using maximum likelihood estimation, with random intercepts at the levels of the region (north/south India) and subject (right/left eye) was used in the comparison between patients with AOD <25 years and ≥25 years, and between N-STDR and STDR groups. Bivariate and multivariate mixed-effects regression analyses were used to evaluate risk factors for STDR in both groups. Odds ratio (OR) and 95% confidence intervals (CIs) were estimated by multilevel logistic regression. A P value of < 0.05 was considered statistically significant.

Results

A total of 654 individuals with DR were included in the study: 161 people (307 eyes) in Group 1 (AOD <25 years) and 493 people (927 eyes) in Group 2 (AOD ≥25 years).

Demography and DM status

The median age at the time of the study was significantly lower in Group 1 (33 years with interquartile range, IQR, 28–36 years, mean 32.3 ± 6 years) than in Group 2 (50 years with IQR 39–61 years, 50.5 ± 12.3 years). Median AOD was 18 years (IQR, 13.3–22.2 years, mean 17.4 ± 6 years) in Group 1 and 37 years (IQR, 31.1–46 years, mean 39.4 ± 10.1 years) in Group 2 [Table 1]. Median duration of diabetes was 15 years (IQR, 10–18.6 years) in youth-onset diabetes group and 10 years (IQR, 5–15 years) in the adult-onset diabetes group. The gender distribution was comparable between the groups. Diabetes was not controlled in either group, and median HbA1c was significantly higher in Group 2 (8.4% in Group 1 vs 9.1% in Group 2; P = 0.01). While a significantly higher proportion of individuals in Group 1 were on insulin therapy (97 patients [61.8%]), a higher proportion of patients in Group 2 were on oral antidiabetic medications (276 patients [57.7%]; P < 0.0001).

Diabetic retinopathy

In AOD <25 group, PDR (n = 55, 34%), PDR with HRC (n = 39, 24%), and moderate NPDR (n = 37, 23%) were common presentations. In AOD ≥ 25 group, PDR (n = 165, 33%), moderate (n = 119, 25%), and severe NPDR (n = 78, 16%) were common presentations. At the last follow-up of 12 months, majority of patients in both the groups had PDR (59%, 42/71 in Group 1 and 52%, 106/204 in Group 2; P < 0.001) [Fig. 1]. Almost half of the patients did not have DME in either eye at
presentation (60% and 49% in Groups 1 and 2, respectively). Moderate DME (8% vs 14%; \( P = 0.043 \)) and severe DME (15% vs 23%; \( P = 0.043 \)) were significantly common in Group 2. DR and DME distributions in both groups at baseline and 12-month follow-up are shown in Table 2.

The mean baseline presenting best-corrected visual acuity in Group 1 patients was logMAR 0.52 ± 0.09 (Snellen equivalent 6/18) and logMAR 0.47 ± 0.05 (Snellen equivalent 6/15) in Group 2 patients. Over one year follow-up, there was two-line loss of vision (\( P = 0.008 \)) in the eyes of Group 1 to logMAR 0.79 ± 0.21 (Snellen equivalent 6/24). The vision was stable (\( P = 0.23 \)) in Group 2: logMAR 0.51 ± 0.04 (Snellen equivalent 6/18) at 12-month follow-up. Mean baseline CMT was higher in Group 2 patients (344 ± 9 \( \mu \)m) than in Group 1 patients (310 ± 17 \( \mu \)m), but the difference was statistically not significant (\( P = 0.07 \)). Mean CMT measurements at 12-month follow-up were higher in Group 2 (332 ± 13 \( \mu \)m) than in Group 1 patients (289 ± 13 \( \mu \)m); however, these differences were not statistically significant [Table 2]. The mean number of laser sittings in each eye in both groups was comparable (2.2 ± 0.4 in Group 1 and 2.2 ± 0.3 in Group 2). Mean number of intravitreal injections were 1.2 ± 0.1 and 1.6 ± 0.3 (\( P = 0.04 \)) and number of vitreoretinal interventions at 1.2 ± 0.1 and 1.2 ± 0.04 (\( P = 0.22 \)), respectively, were comparable.

**Intra- and Intergroup group analysis**

Intragroup analysis showed that both the groups with STDR showed longer duration of DM (Group 1 AOD < 25: 14.9 ± 0.6 years and Group 2 AOD ≥ 25: 11.4 ± 0.7 years). Both the groups with STDR had significantly higher SBP (Group 1 AOD < 25: 134.7 ± 2.3 mmHg and Group 2 AOD ≥ 25: 142.0 ± 1.3 mmHg). Current age, gender, age at diagnosis, and diastolic BP did not have any significant correlation [Table 3].

Further, the bivariate analysis showed a significant association of higher SBP with STDR (odds ratio (OR)

---

**Table 1: Baseline characteristics of individuals with diabetic retinopathy in young and older onset diabetes mellitus**

| Variables                          | Group 1: AOD <25 years (n=161) | Group 2: AOD ≥25 years (n=493) | \( P \)  |
|------------------------------------|---------------------------------|--------------------------------|--------|
| Age at time of study (years), median (IQR) | 33 (28-36)                      | 50 (39-61)                      | <0.0001|
| Gender Male:Female                  | 98:53 (65%:35%)                 | 348:127 (73%:27%)              | 0.06   |
| Age at diagnosis of DM (years), median (IQR) | 18 (13.3-22.2)                 | 37 (31.1-46)                    | <0.0001|
| Duration of DM (years), median (IQR) | 15 (10-18.6)                    | 10 (5-15)                      | <0.0001|
| Duration of hypertension (months), median (IQR) | 20.5 (6-48)                    | 20 (10-84)                     | 0.005  |
| HbA1c (%) , median (IQR)            | 8.4 (7.3-9.8)                   | 9.1 (8.10-2.2)                 | 0.01   |
| Systolic blood pressure (mmHg), median (IQR) | 128 (120-140)                  | 140 (130-150)                  | <0.0001|
| Diastolic blood pressure (mmHg), median (IQR) | 80 (70-90)                     | 80 (80-90)                     | 0.03   |

AOD: age of diabetes; DM: diabetes mellitus; IQR: inter-quartile range

**Table 2: Baseline and follow-up data on disease severity, visual acuity, and optical coherence tomography parameters of individuals with diabetic retinopathy in young and older onset diabetes mellitus**

| Disease severity | Group 1: AOD <25 years | Group 2: AOD ≥25 years | \( P \)  | Group 1: AOD <25 years | Group 2: AOD ≥25 years | \( P \)  |
|------------------|-------------------------|------------------------|--------|-------------------------|------------------------|--------|
| DR Grade         |                         |                        |        |                         |                        |        |
| Mild NPDR        | 14 (9)                  | 68 (14)                | 0.08   | 5 (7)                    | 22 (11)                | 0.49   |
| Moderate NPDR    | 37 (23)                 | 119 (25)               | 0.77   | 12 (17)                  | 38 (19)                | 0.97   |
| Severe NPDR      | 15 (9)                  | 78 (16)                | 0.036  | 12 (17)                  | 38 (19)                | 0.97   |
| PDR              | 55 (34)                 | 165 (34)               | 0.92   | 24 (34)                  | 94 (46)                | 0.045  |
| PDR with HRC     | 39 (24)                 | 56 (12)                | 0.0001 | 18 (25)                  | 12 (6)                 | 0.0001 |
| DME grade        |                         |                        |        |                         |                        |        |
| No DME           | 87 (60)                 | 227 (49)               | 0.013  | 20 (40)                  | 86 (44)                | 0.63   |
| Mild DME         | 23 (16)                 | 69 (15)                | 0.75   | 14 (28)                  | 52 (27)                | 0.84   |
| Moderate DME     | 12 (8)                  | 63 (14)                | 0.09   | 10 (20)                  | 30 (15)                | 0.43   |
| Severe DME       | 22 (15)                 | 105 (23)               | 0.043  | 6 (12)                   | 27 (14)                | 0.61   |
| STDR patients    | 122 (76)                | 358 (73)               | 0.57   | 56 (78)                  | 169 (77)               | 1.00   |
| BCVA (logMAR), mean±SE |            |                        |        |                         |                        |        |
| Baseline         | 0.52±0.09               | 0.47±0.05              | 0.55   | 0.79±0.21               | 0.51±0.04              | 0.14   |
| OCT CMT (µm), mean±SE |            |                        |        |                         |                        |        |
| Baseline         | 310±17                  | 344±9                  | 0.07   | 289±13                  | 332±13                 | 0.09   |

AOD: age of diabetes; BCVA: best-corrected visual acuity, CMT: central macular thickness; DR: diabetic retinopathy; DME: diabetic macular edema; HRC: high-risk characteristics; NPDR: nonproliferative diabetic retinopathy; OCT: optical coherence tomography; PDR: proliferative diabetic retinopathy; STDR: sight-threatening diabetic retinopathy; SE: standard error
In Group 1 patients, the bivariate analysis showed a significant association of lower age at diagnosis of DM, longer duration of DM, and higher SBP with STDR, but on multivariate analysis, only longer duration of diabetes (OR 1.073 ± 0.023; \( P = 0.001 \)) and higher SBP (OR 1.029 ± 0.010; \( P = 0.002 \)) were significant risk factors [Fig. 2]. Table 4 compares the significance of the association of risk factors for STDR in Group 2 compared to Group 1. Multivariate analysis showed that the only difference between the groups was that Group 2 patients were older, and the duration of diabetes was shorter.

### Discussion

People with young onset of diabetes live with a longer duration of hyperglycemia and are therefore predisposed to a greater risk for microvascular complications of diabetes.\(^2,3\) This study found poor glycemic control in either group, PDR with HRC in younger onset DM group, and severe DME in adult-onset DM group. An association of higher SBP with STDR in both groups and longer duration of diabetes with STDR in adult-onset DM was noted. Both groups have a male preponderance (65% and 73%). This is different from the female predominance observed in the SEARCH (USA) cohort.\(^4\)

In our cohort, irrespective of the age of onset of diabetes, higher HbA1c predisposed to STDR. The importance of HbA1c association with DR has been highlighted in numerous studies. The severity of DR is shown to increase with an increase in HbA1c levels.\(^15-18\) In this study, all individuals had varying severity of DR. As shown in earlier studies, a longer duration of DM along with uncontrolled blood sugar has predisposed
Table 4: Comparison of risk factors for sight-threatening diabetic retinopathy between the groups: age of diabetes under and above 25

| Variable                                      | Group 1: AOD <25 STDR n=122 patients (39.7%) | Group 2: AOD ≥25 STDR n=358 patients (38.6%) | P   |
|-----------------------------------------------|---------------------------------------------|-----------------------------------------------|-----|
| Age at presentation (years), mean±SE          | 32.4±1.0                                    | 50.3±0.6                                      | <0.0001 |
| Male (%)                                      | 66%                                         | 73%                                          | 0.15 |
| Age at DM diagnosis (years), mean±SE          | 17.4±0.8                                    | 38.8±0.5                                     | <0.0001 |
| Duration of DM (years), mean±SE              | 14.4±1.2                                    | 11.0±1.0                                     | 0.0001 |
| HbA1c (%), mean±SE                            | 9.4±0.3                                     | 8.8±0.2                                      | 0.046 |
| Treatment                                     |                                             |                                              |     |
| OHA                                           | 28%                                         | 58%                                          | <0.0001 |
| Insulin                                       | 66%                                         | 22%                                          | <0.0001 |
| OHA + Insulin                                 | 2%                                          | 16%                                          | 0.0006 |
| Systolic BP (mmHg), mean±SE                   | 134.7±2.5                                   | 142.0±1.4                                    | 0.01 |
| Diastolic BP (mmHg), mean±SE                  | 81.9±1.2                                    | 83.6±0.7                                     | 0.23 |

AOD: age of diabetes; BP: blood pressure; DM: diabetes mellitus; OHA: oral hypoglycemic drugs; STDR: sight threatening diabetic retinopathy; SE: standard error.

Strict blood sugar control is key to reduce the incidence of diabetic retinopathy. Glycated hemoglobin of ≤7% is recommended and needs 3 monthly testing to monitor the status of diabetes control. Poor diabetes control in Indian subjects is not a new observation; in a recent large hospital-based study across India (SPEED study; 11,390 people known diabetes), only 32.1% people had satisfactory diabetes control, and only 11.1% people were regular in testing HbA1c. Thus, it requires greater advocacy among the people with diabetes in India for good control of diabetes and use the proper test to assess the status of diabetes control.

DME is an important cause of visual impairment in people with diabetes. Some of the important risk factors are longer duration of diabetes, poor glycemic control, and elevated BP. In the current study, people with AOD above 25 had a higher prevalence of severe DME than people in the AOD under 25 (23% vs. 15%). They had a longer duration of diabetes and higher SBP than the people AOD under 25 group. The trend is similar to earlier studies. Study by Klein et al. had shown that the incidence of DME was higher in patients with age at DM diagnosis after 30 years (39.3%) when compared to patients diagnosed before age 30 years (20.1%). Thus, the proportion of eyes with STDR was similar in both groups. Our study has shown that there were significant differences in the duration of diabetes and treatment for diabetes, SBP, and hyperglycemia in those with STDR in both groups. However, there were no differences between the groups in the modifiable risk factors. Young-onset type 2 diabetes could be as aggressive as type 1 diabetes in causing STDR. Among individuals with young-onset diabetes (AOD below 25 years) with a longer duration of diabetes (over 15 years), 44% of individuals with type 1 diabetes and 52% of individuals with youth-onset type 2 DM had STDR. The study by Rajalakshmi et al. showed that young-onset type 2 diabetes is as aggressive as type 1 diabetes in causing STDR. In the same study, individuals with duration of diabetes over 15 years STDR was present in 44% of young-onset type 1 diabetes and 52% of individuals with young-onset type 2 diabetes. The SPEED study, a multicentric study done across 14 eye care facilities in India, also reported that in individuals with adult-onset diabetes with duration of diabetes over 15 years, STDR was reported in 34%. Longer duration of diabetes is the key nonmodifiable risk factor. It again emphasizes the regular screening of DM patients for early detection of DR and DME to avoid vision loss.

The treatment characteristics like mean number of PRP laser sittings, intravitreal injections, and vitrectoreintal interventions were almost equal in both groups. The affection of vision was more in the youth-onset DM group over one year, whereas the older cohort showed a stable vision for one year follow-up. This goes against the observations made in the West, where visual impairment has shown recent declining trends in the individuals who have been diagnosed with DM at less than 30 years of age. This was attributed to a better implementation of clinical protocols such as dilated eye examination to detect and manage vision-threatening DR and measures to enhance glycemic control.

To study the influence of age and other factors on the severity of DR, risk factors analysis was done in both groups. Both the groups at presentation had majority of them affected with STDR. Higher SBP found to be a significant risk for developing STDR in both youth onset and older onset DM groups. In addition, duration of DM was associated with high risk of developing STDR in older onset DM group.

Hypertension is one among the potential risk factors for the occurrence and progression of DR. Elevated BP affects hemodynamic and vascular endothelial growth factor (VEGF) induced pathways in DR. Elevated BP upregulates VEGF expression in retinal endothelial cells and worsens the DR. United Kingdom Prospective Diabetes Study (UKPDS) had shown that patients with good control of BP (<150/85 mmHg) had a 34% reduction in severity of retinopathy and 47% decreased risk in worsening of visual acuity. Similarly, in our study, SBP was uncontrolled in both groups with STDR with older onset DM having higher range of uncontrolled BP (142.0 ± 1.4 mmHg). This indicates strict control of SBP and also at lower range than what was proposed in UKPDS study before to reduce the risk of STDR. A study by Okudaira et al. has shown the role of elevated BP in progression to PDR.
in young-onset type 2 diabetes. The findings of our study demonstrate the risk of developing STDR with higher SBP, indicating the need to control modifiable risk factors such as hypertension.\(^{[30]}\) A lower SBP (140 mmHg) and lower DBP (70 mmHg) combined with good metabolic control has been shown to reduce the occurrence of STDR and also in reducing the progression of DR\(^{[37,38]}\). In the current cohort, the duration of hypertension was at least 20 months, and 56.2% (222/395) of the patients had hypertension. Hypertension was the only modifiable risk factor in Group 1 and Group 2, with no significant differences between groups. Therefore, BP control should be emphasized equally to all people with diabetes, irrespective of their age or duration of diabetes.

The strengths of our study include that it is possibly the first multicentric study from India (involving 14 tertiary care eye facilities across India with large sample size) comparing the clinical profile and risk factors associated with DR and STDR in youth onset DM versus older onset DM. This real-time data analysis of DR and DME characteristics and analysis of risk factors for STDR in relation to the age at onset of DM have provided an insight into the burden of PDR with HRC/STDR in India in individuals with young onset as well older onset diabetes.

Limitations of the study are: there has been no control arm of individuals without DR for comparison of the systemic parameters of those with and without DR. It is clinic-based data; the results cannot be extrapolated to the population. The data of patients are from tertiary eye care facilities where people might have presented with advanced DR for treatment; it is likely that the proportion of STDR is skewed. This has been a retrospective analysis with a review of medical records in eye hospitals with nonavailability of all of the biochemical parameters to support the diagnosis of the type of diabetes (type 1 DM). As the systemic parameters were not available during follow-up, a causal relationship cannot be established based on the data.

**Conclusion**

In this multicenter study done across various tertiary eye care facilities in India, we found that PDR and PDR with HRC were more prevalent in individuals with AOD under 25, and severe DME was more common in individuals with AOD above 25 years. Patients with young-onset diabetes had a more visual loss on follow-up with two-line reduction in visual acuity. Raised SBP and poor glycemic control increased the risk of STDR in every age group. Keeping in mind the increasing number of people with diabetes, India needs greater advocacy to control risk factors of STDR by timely screening and early treatment of STDR to avoid reversible visual impairment.

**Financial support and sponsorship**

Hyderabad Eye Research Foundation, Hyderabad, India (DCP, UCB, AM, TD, PKR) and Ornate India GCRF/UKRI funding (MR/P207881/1), UK.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Hockett CW, Praveen PA, Ong TC, Amutha A, Isom SP, Jensen ET, et al. Clinical profile at diagnosis with youth-onset type 1 and type 2 diabetes in two pediatric diabetes registries: SEARCH (United States) and YDR (India). Pediatr Diabetes 2021;22:22-30.

2. Praveen PA, Madhu SV, Mohan V, Das S, Katki S, Shah N, et al. Registry of youth onset diabetes in India (YDR) rationale, recruitment, and current status. J Diabetes Sci Technol 2016;10:1034-41.

3. Praveen PA, Madhu SV, Viswanathan M, Das S, Katki S, Shah N, et al. Demographic and clinical profile of youth onset diabetes patients in India—Results from the baseline data of a clinical based registry of people with diabetes in India with young age at onset—[YDR-02]. Pediatr Diabetes 2021;22:15-21.

4. Mayer-Davis EJ, Davis C, Saadine J, D’Agostino Jr R, Dabelea D, Dolan L, et al. Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: A pilot study. Diabet Med 2012;29:1148-52.

5. Amutha A, Ranjit U, Anjana RM, Shanthi R CS, Rajalakshmi R, Venkatesan U, et al. Clinical profile and incidence of microvascular complications of childhood and adolescent onset type 1 and type 2 diabetes seen at a tertiary diabetes center in India. Pediatr Diabetes 2021;22:67-74.

6. Venkatesh P, Tibrewal S, Bhownik D, Tripathi M, Ramakrishnan S, Vashist N, et al. Prevalence of systemic co-morbidities in patients with various grades of diabetic retinopathy. Indian J Med Res 2014;140:77-83.

7. Shah K, Gandhi A, Natarajan S. Diabetic retinopathy awareness and associations with multiple comorbidities: Insights from DIAMOND study. Indian J Endocrinol Metab 2018;22:30-5.

8. Iglay K, Hannachi H, Joseph Howie P, Xu J, Li X, Engel SS, et al. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. Curr Med Res Opin 2016;32:1243-52.

9. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The All India Ophthalmological Society diabetic retinopathy eye screening study 2014. Indian J Ophthalmol 2016;64:38-44.

10. Raman R, Ganesan S, Pal SS, Gella L, Kulothungan V, Sharma T. Incidence and progression of diabetic retinopathy in urban India: Sankara nethralaya-diabetic retinopathy epidemiology and molecular genetics study (SN-DREAMS II), Report 1. Ophthalmic Epidemiol 2017;24:294-302.

11. Raman R, Ganesan S, Pal SS, Kulothungan V, Sharma T. Prevalence and risk factors for diabetic retinopathy in rural India. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study III (SN-DREAMS III), Report No 2. BMJ Open Diabetes Res Care 2014;2:e000005.

12. Raman R, Gupta A, Kulothungan V, Sharma T. Prevalence and risk factors of diabetic retinopathy in subjects with suboptimal glycemic, blood pressure and lipid control. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, Report 33). Curr Eye Res 2012;37:513-23.

13. Raman R, Rani PK, Racchepalle SR, Gnanamoorthy P, Uthra S, Kumaramanickavel G, et al. Prevalence of diabetic retinopathy in India: Sankara Nethralaya diabetic retinopathy epidemiology and molecular genetics study report 2. Ophthalmology 2009;116:311-8.

14. Wilkinson C, Ferris FL 3rd, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110:1677-82.

15. Diabetes Control and Complications Trial Research Group; Nathan DM, Gennuth S, Lachin J, Cleary P, Cromoff O, Davis M, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-86.

16. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837-53.

17. Colagrucci S, Lee CM, Wong TY, Balkau B, Shaw J, Borch-Johnsen K,
et al. Glycemic thresholds for diabetes-specific retinopathy: Implications for diagnostic criteria for diabetes. Diabetes Care 2011;34:145-50.
18. Feng R-F, Liu H-Y, Liu Y-L, Xu Q, Qiao L, Gong C-J, et al. Diabetes onset at an earlier age and high HbA1c levels as risk factors of diabetic retinopathy. Int J Ophthalmol 2021;14:269-76.
19. Roy MS, Klein R, O'Colmain BJ, Klein BE, Moss SE, Kempen JH. The prevalence of diabetic retinopathy among adult type 1 diabetic persons in the United States. Arch Ophthalmol 2004;122:546-51.
20. Rajalakshmi R, Prathiba V, Mohan V. Does tight control of systemic factors help in the management of diabetic retinopathy? Indian J Ophthalmol 2016;64:62-8.
21. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan DM, Peterson CM, et al. Tests of glycemia in diabetes. Diabetes Care 2003;26(Suppl 1):S106-8.
22. Das T, Behera UC, Bhattacharjee H, Gilbert C, Murthy GV, Rajalakshmi R, et al. Spectrum of eye disorders in diabetes (SPEED) in India: Eye care facility based study. Report # 1. Eye disorders in people with type 2 diabetes mellitus. Indian J Ophthalmol 2020;68(Suppl 1):S16-20.
23. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond) 2015;2:17.
24. Klein R, Klein BE. Vision disorders in diabetes. Diabetes in America. 1995;6:1-293.
25. Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: Pathogenesis and treatment. Surv Ophthalmol 2009;54:1-32.
26. Wenick AS, Bressler NM. Diabetic macular edema: Current and emerging therapies. Middle East Afr J Ophthalmol 2012;19:4-12.
27. Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin epidemiologic study of diabetic retinopathy XV: The long-term incidence of macular edema. Ophthalmology 1995;102:7-16.
28. Rajalakshmi R, Behera UC, Bhattacharjee H, Das T, Gilbert C, Murthy GV, et al. Spectrum of eye disorders in diabetes (SPEED) in India. Report # 2. Diabetic retinopathy and risk factors for sight threatening diabetic retinopathy in people with type 2 diabetes in India. Indian J Ophthalmol 2020;68(Suppl 1):S21-6.
29. 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.
30. Rajalakshmi R, Shanthirani CS, Amutha Anandakumar RM, Murthy G, Gilbert C, Mohan V. Assessment of diabetic retinopathy in type 1 diabetes in a diabetes care center in South India—Feasibility and awareness improvement study. Indian J Ophthalmol 2020;68(Suppl 1):S92-5.
31. Hovind P, Tarnow L, Rossing K, Rossing P, Eising S, Larsen N, et al. Decreasing incidence of severe diabetic microangiopathy in type 1 diabetes. Diabetes Care 2003;26:1258-64.
32. Klein R, Lee KE, Knudtson MD, Gangnon RE, Klein BE. Changes in visual impairment prevalence by period of diagnosis of diabetes: The Wisconsin Epidemiologic Study of Diabetic Retinopathy. Ophthalmology 2009;116:1937-42.
33. Srivastava B, Rema M. Does hypertension play a role in diabetic retinopathy? J Assoc Physicians India 2005;53:803-8.
34. Srivastava BK, Ramya B, Prathiba V, Mohan V. Systemic factors affecting diabetic retinopathy. J Diabetol 2018;9:73-7.
35. Group UPDS. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998;317:703-13.
36. Okudaira M, Yokoyama H, Otani T, Uchigata Y, Iwamoto Y. Slightly elevated blood pressure as well as poor metabolic control are risk factors for the progression of retinopathy in early-onset Japanese Type 2 diabetes. J Diabetes Complications 2000;14:281-7.
37. Pan C-W, Wang S, Xu C-L, Song E. Combined effect of glycemic and blood pressure control on diabetic retinopathy among Chinese with type-2 diabetes mellitus. Diabetol Metab Syndr 2018;10:73.
38. Pesin N, Mandelcorn ED, Felfeli T, Ogilvie RI, Brent MH. The role of occult hypertension in retinal vein occlusions and diabetic retinopathy. Can J Ophthalmol 2017;52(Suppl 1):S30-3.