Original Article

Comparison of Progression of Diabetic Retinopathy among Young-Onset and Late-Onset Diabetes Mellitus

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Abstract

Background*: Diabetic retinopathy (DR) is a major microvascular complication of diabetes mellitus (DM) and a leading cause of vision loss globally. The rate of progression of DR may differ between individuals diagnosed with diabetes at a younger age (young-onset diabetes mellitus, YODM) and those diagnosed later in life (late-onset diabetes mellitus, LODM).*

Objective*: This study aims to compare the progression patterns of DR in YODM and LODM patients, evaluating differences in severity, risk factors and clinical outcomes.*

Methods and Materials*: This retrospective cohort study analyzed medical records of patients diagnosed with diabetes for at least five years at Vitreo Retina Department of National Institute of Ophthalmology & Hospital, Dhaka in 2017 & 2018. Participants were categorized into two groups: YODM: Diagnosed before the age of 40 years & LODM: Diagnosed at or after the age of 40 years. Demographic and clinical data, including age at diagnosis, diabetes duration, HbA1c levels, blood pressure, lipid profile and treatment history, were collected. Comparisons between YODM and LODM groups were performed using chi-square tests for categorical variables and t-tests for continuous variables.*

Results*: 45.0% of YODM patients had progressed to PDR compared to 27.0% of LODM patients ($p<0.001$). DME was observed in 38.0% of YODM cases versus 22.0% in LODM cases ($p=0.002$). YODM patients exhibited higher mean HbA1c levels (8.9±1.3%) than LODM patients (7.8±1.1%, $p=0.015$). Poor glycemic control was strongly correlated with DR severity in both groups. LODM patients had a higher prevalence of hypertension (68.0% vs. 45.0%, $p<0.001$) and dyslipidemia (52.0% vs. 40.0%, $p=0.012$), which were associated with DR progression. However, despite more comorbidities, DR severity was lower in LODM, possibly due to shorter disease duration. Intravitreal anti-VEGF injections were required in 35.0% of YODM patients versus 20.0% of LODM patients. Laser photocoagulation was more frequentlyneeded in YODM (28.0%) than in LODM (15.0%).*

Conclusions*: This study highlights that DR progresses more aggressively in YODM patients despite similar diabetes duration when compared to LODM patients. The increased risk appears to be driven primarily by prolonged hyperglycemic exposure and poorer metabolic control. In contrast, LODM patients, despite a higher burden of systemic comorbidities, exhibit slower DR progression.*

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by prolonged hyper-glycemia, leading to micro-vascular and macro-vascular complications. One of the most significant microvascular complications is diabetic retinopathy (DR), which affects nearly one-third of all individuals with diabetes and remains a leading cause of vision loss worldwide[1,2]. The progression of DR is influenced by several factors, including glycemic control, blood pressure, lipid levels and the duration of diabetes[3,4]. The age at onset of diabetes plays a crucial role in determining the disease burden and the severity of its complications Patients diagnosed at a younger age (young-onset diabetes mellitus, YODM) experiencea longer cumulative exposure to hyperglycemia,which increasestheir risk for more aggressive micro-vascular damage and early progression to sight-threatening DR[5,6]. Several studies indicatethat YODM patients exhibit higher rates of diabetic

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complications, including nephropathy, neuropathy and retinopathy, due to prolonged disease duration and often poorer glycemic control[7,8]. Conversely, late-onset diabetes mellitus (LODM) is commonly associated with a higher prevalence of systemic comorbidities, such as hypertension, dyslipidemia and cardiovascular disease, which can influence DR progression via mechanisms like endothelial dysfunction and increased vascular permeability[9,10]. While LODM patients generally have a shorter duration of hyperglycemia exposure, the presence of additional risk factors, such as insulin resistance and systemic inflammation, mayaccelerate micro-vasculardamage[11]. Despite the growing body of evidence on DR risk factors, comparative data on the progression of DR in YODM versus LODM remains limited. Understanding how DR progresses in these two distinct patient populations is critical for optimizing screening protocols, tailoring management strategies and preventing vision loss. This study aims to compare the severity and progression of DR in YODM and LODM patients, focusing on the impact of glycemic control, comorbidities and therapeutic interventions to guide evidence-based clinical practice.

Methods

This retrospective cohort study analyzed medical records of 2017 & 2018 patients diagnosed with diabetes for at least five years at Vitreo Retina Department of National Institute of Ophthalmology & Hospital, Dhaka. Participants were categorized into two groups:

•YODM: Diagnosed before the age of 40 years.

•LODM: Diagnosed at or after the age of 40 years.

Inclusion criteria included confirmed diagnosis of DR through fundus photography and optical coherence tomography (OCT). Patients with secondary diabetes or other retinal diseases were excluded. Demographic and clinical data, including age at diagnosis, diabetes duration, HbA1c levels, blood pressure, lipid profile and treatment history, were collected. DR severity was classified using the International Clinical Diabetic Retinopathy Severity Scale into mild non-proliferative DR (NPDR), moderate NPDR, severe NPDR and proliferative DR (PDR). Diabetic macular edema (DME) presence was also assessed. Comparisons between YODM and LODM groups were performed using chi-square tests for categorical variables and t-tests for continuous variables. Multivariate logistic regression was conducted to identify independent risk factors for DR progression.

Results

A total of 400 patients (200 YODM, 200 LODM) were included. The mean age at diabetes diagnosis was 32.5±4.8 years in YODM and 55.7±6.2 years in LODM. The mean duration of diabetes at study entry was similar between groups (15.2±3.9 years for YODM vs.14.8±4.1 years for LODM, p=0.

Table I: Baseline Characteristics

Characteristic	YODM (n=200)	LODM (n=200)	p value
Mean age at diagnosis (years)	32.5±4.8	55.7±6.2	
Mean diabetes duration (years)	15.2±3.9	14.8±4.1	0.42

Table II: Diabetic Retinopathy Severity and Progression

Severity/progession	YODM (%)	LODM (%)	p value
Progression to PDR	45.0	27.0	<0.001
Presence of DME	38.0	22.0	0.002

Table III: Association with Glycemic Control

Glycemin control factor	YODM	LODM	p value
Mean HbA1c (%)	8.9±1.3	7.8±1.1	0.015
Correlation with DR severity	Strong	Strong	-

Table IV: Impact of Comorbidities

Comorbidity	YODM (%)	LODM (%)	p value
Hypertension	45.0	68.0	<0.001
Dyslipidemia	40.0	52.0	0.012

Table V: Therapeutic Interventions

Intervention	YODM (%)	LODM (%)
Intravitreal anti-VEGF	35.0	20.0
Laser photocoagulation	28.0	15.0

Faster Progression in YODM:
•45% of YODM patients had progressed to PDR compared to 27% of LODM patients (p<0.001).
•DME was observed in 38% of YODM cases versus 22% in LODM cases (p=0.002).
Association with Glycemic Control:
•YODM patients exhibited higher mean HbA1c levels (8.9±1.3%) than LODM patients (7.8±1.1%, p=0.015).
•Poor glycemic control was strongly correlated with DR severity in both groups.
Impact of Comorbidities:
•LODM patients had a higher prevalence of hypertension (68.0% vs. 45.0%, p<0.001) and
•dyslipidemia (52.0% vs. 40.0%, p=0.012), which were associated with DR progression.
•However, despite more comorbidities, DR severity was lower in LODM, possibly due to shorter disease duration.
Therapeutic Interventions:
•Intravitreal anti-VEGF injections were required in 35% of YODM patients versus 20% of LODM patients.
•Laser photocoagulation was more frequently needed in YODM (28%) than in LODM (15%).

Discussion

Our study highlights significant differences in the progression of diabetic retinopathy (DR) between young-onset diabetes mellitus (YODM) and late-onset diabetes mellitus (LODM) patients. Despite a similar duration of diabetes at study entry, YODM patientsexhibited a more rapid and severe progression of DR, with a higher prevalence of proliferative diabetic retinopathy (PDR) and diabetic acular edema (DME). Several key factors, including glycemic control, comorbidities and therapeutic interventions, werefound to influence these outcomes. Our results demonstrate that 45.0% of YODM patients progressed to PDR, compared to only 27.0% of LODM patients (p<0.001). Similarly, DME was more common in YODM (38.0% vs. 22.0%, p=0.002). These findings are consistent with previous studies indicating that patients diagnosed with diabetes at a younger age tend to experience longer cumulative exposure to hyperglycemia, which accelerates microvascular complications[5,11]. The prolonged exposure to elevated glucose levels may contribute to increased oxidative stress, inflammation and retinal microvascular damage6. A key finding in our study was that YODM patients had higher mean HbA1c levels (8.9±1.3%) compared to LODM patients (7.8±1.1%, p=0.015). Poor glycemic control was strongly correlated with DR severity in both groups. This is in line with findings from the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), both of which demonstrated that higher HbA1c levels are associated with increased DR progression isk[6,9]. Intensive glycemic control has been shown to significantly reduce the progression of DR by limiting endothelial dysfunction and reducing retinal vascular permeability[3]. Interestingly, while LODM patients exhibited a higher prevalence of hypertension (68.0% vs. 45.0%, p<0.001) and dyslipidemia (52.0% vs. 40.0%, p=0.012), DR severity was lower in this group. This may be due to the shorter duration of hyperglycemia exposure before DR onset. Studies suggest that hypertension and dyslipidemia contribute to DR progression by impairing retinal autoregulation and promoting vascular leakage[10]. However, in LODM, the relatively shorter disease duration may offset these risk factors, leading to less aggressive DR progression compared to YODM. This study also found that YODM patients required more aggressive treatment strategies, with 35.0% receivingintravitreal anti-VEGF therapy compared to 20.0% of LODM patients and 28.0% requiring laser photocoagulation compared to 15.0% in LODM. This aligns with previous studies that report increased treatment demand in younger patients due to the more aggressive disease course[12]. The need for earlier and more frequent interventions in YODM highlights the importance of strict metabolic control and regular ophthalmologic monitoring. Early and More Frequent Screening for YODM Patients: Given their increased risk of rapid progression to PDR and DME, YODM patients should undergo more intensive ophthalmologic surveillance. Current guidelines recommend annual retinal examinations, but our findings suggest that high-risk YODM individuals may benefit frombiannual screening[2].

1.Glycemic Control Strategies:
Since hyperglycemia is a major driver of DR progression, personalized HbA1c targets should be set for YODM patients to mitigate long-term complications.
2.Comorbidity Management in LODM:
Although DR progression is slower in LODM, hypertension and dyslipidemia remain significant contributors. Strict blood pressure and lipid control are essential to prevent future complications.

Conclusion

This study highlights that DR progresses more aggressively in YODM patients despite similar diabetes duration when compared to LODM patients. The increased risk appears to be driven primarily by prolonged hyperglycemic exposure and poorer metabolic control. In contrast, LODM patients, despite a higher burden of systemic comorbidities, exhibit slower DR progression, likely due to their shorter cumulative exposure to hyperglycemia. These findings emphasize the need for early screening, stricter metabolic control and tailored treatment strategies based on age at diabetes onset.

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