IDENTIFICATION OF THE RISK FACTORS FOR SIGHT THREATING DIABETIC RETINOPATHY PRESENTING IN A TERTIARY EYE HOSPITAL

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ABSTRACT

Diabetic retinopathy (DR) is a leading cause of blindness among working-age populations globally, with sight-threatening diabetic retinopathy (STDR) which includes diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). So identifying the predominant risk factors is vital for targeted screening and prevention.This study aims to find the independent risk factors associated with the development of sight-threatening DR (STDR). A case-control study was conducted involving 50 type II diabetic patients. The case group (n=28) comprised patients diagnosed with DME or PDR, while the control group (n=22) consisted of diabetic patients with no diabetic retinopathy (NO DRP) or mild NPDR. Data on age, sex, diabetes duration (DM), hypertension (HTN), fasting blood sugar, postprandial blood sugar, and HbA1c were collected. Univariate and multiple logistic regression analyses were performed to calculate crude and adjusted odds ratios (ORs). In univariate analysis, DM duration (OR=1.19, 95% CI: 1.09-1.30, p<0.001), HbA1c (OR=3.87, 95% CI: 1.84-8.15, p<0.001), and postprandial blood sugar (OR=1.10 per 10 mg/dL, 95% CI: 1.01-1.20, p=0.035) were significant risk factors. However, in the multiple logistic regression model adjusting for all covariates, only DM duration remained a statistically significant independent predictor (Adjusted OR=1.20, 95% CI: 1.08-1.34, p=0.001). Patients with diabetes for over 10 years had a twelve-fold increased odds of STDR (OR=12.0, 95% CI: 2.70-53.3) compared to those with less than 5 years' duration. Duration of diabetes is the strongest independent risk factor for sight-threatening diabetic retinopathy. While glycemic control is important, long-term exposure to the diabetic milieu appears to be the primary driver of disease progression. These findings underscore the critical need for intensified ophthalmologic surveillance in patients with long-standing diabetes.

KEYWORDS

Diabetes duration, diabetic macular edema, HbA1c, hypertension, proliferative diabetic retinopathy

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INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of blindness among working-age populations with sight-threatening diabetic retinopathy (STDR) accounting 28.54 million in 2020 globally.[1] In Nepal, the prevalence of DR is 23.8%, with STDR—encompassing proliferative DR (PDR), and clinically significant macular edema—posing significant challenges despite therapeutic advances.[2,3] Risk factors such as prolonged diabetes duration (>5 years), poor glycemic control (elevated HbA1c), hypertension, and limited healthcare access have been identified in global studies.[4,5] This study aims to bridge this gap by identifying risk factors for STDR, enabling targeted interventions to reduce blindness and alleviate healthcare burdens.

While the correlation between hyperglycemia and DR risk is well-documented in large prospective studies like the DCCT and UKPDS,[6,7] the relative contribution of different risk factors, particularly in the context of modern clinical practice, warrants further investigation. Specifically, understanding which factors retain independent predictive power in a multivariable model is essential for refining risk stratification models and optimizing screening protocols.

This study was done with aims to conduct a case-control analysis to identify the independent risk factors that distinguish patients with sight-threatening DR (DME or PDR) from diabetic patients without retinopathy.

MATERIALS AND METHODS

Study Design and Population: A case-control study was conducted on type II 50 patients with diabetes from July 2024 to March 2025. The study was divided into two groups: Case Group **(**28 patients with a diagnosis of either DME or PDR) and Control Group (22 patients with diabetes with no evidence of diabetic retinopathy (NO DRP) or mild NPDR without DME). Age, Sex, duration of diabetes mellitus (DM in years), and history of hypertension (HTN), coded as a binary variable (Yes/No) were recorded. Fasting blood sugar (mg/dL), postprandial bblood sugar (mg/dL), and glycated hemoglobin (HbA1c, %) were noted. The study was approved by the Nepal Heath Research Council (Ref.: 2467/2024).

Statistical Analysis: Statistical analyses were performed using SPSS-21. Group comparisons used T-tests for continuous and Chi-square tests for categorical variables. A two-tailed p-value of <0.05 was considered statistically significant. Unconditional logistic regression was used to calculate crude (univariate) and adjusted (multivariable) Odds Ratios (ORs) with 95% Confidence Intervals (CIs). The multivariable model included all studied variables: Duration of DM, duration of hypertension, fasting blood sugar (mg/dL), postprandial blood sugar (mg/dL), and glycated hemoglobin (HbA1c, %).

RESULTS

Baseline Characteristics: The baseline characteristics of the cases and controls are summarized in Table 1. The two groups were well-matched for age (56.4 vs. 58.0 years, p=0.587) and sex distribution (50.0% vs. 54.5% male, p=0.749). However, cases had a significantly longer duration of diabetes (13.6 vs. 6.5 years, p<0.001) and a higher prevalence of hypertension (57.1% vs. 31.8%, p=0.072), though the latter was of borderline significance. Metabolic parameters were worse in the case group, with significantly higher HbA1c (8.1% vs. 6.5%, p<0.001) and postprandial blood sugar levels (234.2 vs. 177.5 mg/dL, p=0.038).

Univariate analysis of risk factors: The results of the univariate logistic regression are shown in Table 2. Diabetes duration was a potent risk factor, with each additional year conferring a 19% increase in the odds of STDR (OR=1.19, p<0.001). HbA1c was also a strong predictor, with each 1% increase associated with nearly a four-fold increase in odds (OR=3.87, p<0.001).

Table 1: Baseline characteristics of study participants

Characteristic	Cases (n=28)	Controls (n=22)	p-value
Age, years (Mean ± SD)	56.4 ± 9.8	58.0 ± 10.9	0.587
Male Sex, n (%)	14 (50.0)	12 (54.5)	0.749
DM duration, years (Mean ± SD)	13.6 ± 6.7	6.5 ± 6.3	**<0.001**
Hypertension, n (%)	16 (57.1)	7 (31.8)	0.072
BS fasting, mg/dL (Mean ± SD)	152.6 ± 75.2	126.6 ± 23.8	0.104
BS postprandial, mg/dL (Mean ± SD)	234.2 ± 127.3	177.5 ± 44.8	**0.038**
HbA1c, % (Mean ± SD)	8.1 ± 2.0	6.5 ± 0.5	**<0.001**

Table 2: Univariate analysis (Crude odds ratios)

Risk factor	Crude OR	95% CI
DM duration (per year)	1.19	1.09 - 1.30
HbA1c (per 1%)	3.87	1.84 - 8.15
HTN (Yes vs. No)	2.85	0.92 - 8.85
BS postprandial (per 10 mg/dL)	1.10	1.01 - 1.20
BS fasting (per 10 mg/dL)	1.08	0.98 - 1.19
Age (per year)	0.99	0.94 - 1.03
Sex (Male vs. Female)	0.83	0.28 - 2.48

Table 3: Multiple logistic regression analysis (Adjusted odds ratios)

Risk factor	Adjusted OR	95% CI
DM duration (per year)	1.20	1.08 - 1.34
HbA1c (per 1%)	1.24	0.83 - 1.85
HTN (Yes vs. No)	1.44	0.57 - 3.67
BS postprandial (per 10 mg/dL)	1.02	0.94 - 1.10
BS fasting (per 10 mg/dL)	1.05	0.96 - 1.15
Age (per year)	1.00	0.94 - 1.05
Sex (Male vs. Female)	1.26	0.51 - 3.10

Table 4: Risk of STDR by diabetes duration category

DM duration	Cases/Controls	Odds ratio (OR)
<5 years	3 / 10	1.00 (Reference)
5-10 years	7 / 7	3.33
>10 years	18 / 5	12.00

Postprandial blood sugar was a significant but weaker predictor. Hypertension showed a trend towards association (OR=2.85, p=0.070), while age and sex were not significant.

Multiple logistic regression analysis: When all variables were included in a multiple logistic regression model (Table 3), only diabetes duration remained a statistically significant independent predictor of STDR (Adjusted OR=1.20, 95% CI: 1.08-1.34, p=0.001). The effects of HbA1c, hypertension, and postprandial blood sugar were attenuated and lost statistical significance after adjusting for diabetes duration and other confounders.

Table 5: Risk of STDR by HbA1c categories

HbA1c	Cases/controls	Odds ratio (OR)
<7%	7/17	1.00 (Ref)
7-8%	10/5	4.86
>8%	11/0	∞

Stratified and Dose-Response Analysis: The strength of the association with diabetes duration was further illustrated by stratification (Table 4). Compared to patients with less than 5 years of diabetes, those with 5-10 years had a 3.3-fold increased odds, and those with over 10 years had a **12.0-fold increased odds** of STDR (p for trend <0.001).

Model performance: The multiple regression model demonstrated good fit (Hosmer-Lemeshow test, p=0.556) and excellent discriminatory power, with an area under the ROC curve of 0.84. The overall classification accuracy was 74%.

DISCUSSION

Global prevalence of diabetic retinopathy and projection of burden through 2045 report estimated that there will be 103.12 million people with DR and 28.54 million with STDR by 2020[1] and the number of people with DR and STDR is expected to increase to 160.50 million and 44.82 million respectively, by 2045. DR will be socioeconomic burden in the world as it causes increasing number of blindness or sight threatening condition.

This case-control study identifies the duration of diabetes as the most robust and independent risk factor for sight-threatening diabetic retinopathy. While univariate analysis confirmed the expected associations with hyperglycemia (HbA1c, postprandial glucose) and hypertension, these factors did not retain statistical significance in the multivariable model after accounting for diabetes duration. Lui *et al*[10] concluded that duration of diabetes and hyperglycemia are independent risk factors for STDR.[10-15]

The finding that each additional year of diabetes increases the odds of STDR by 20.0% underscores the cumulative, irreversible nature of microvascular damage. The dose-response relationship is striking, with patients suffering from diabetes for over a decade facing a twelve-fold greater risk than those with a shorter disease duration. This aligns with the pathophysiological understanding of DR as a condition driven by long-term exposure to metabolic insults, leading to progressive damage to pericytes, capillary basement membrane thickening, and retinal ischemia.[8]

The attenuation of HbA1c's significance in the multivariable model is a critical observation. It suggests that while poor glycemic control is a key driver of retinopathy, its effect is powerfully mediated through time. In other words, the *long-term history* of glycemic exposure, embodied by the disease duration, may be a more potent predictor of advanced complications than a *cross-sectional measure* of recent control (HbA1c). This does not negate the importance of glycemic control but rather reframes it: optimizing HbA1c is crucial for slowing the onset and progression of retinopathy over the long term.[6,7]

Our findings have direct clinical implications for screening programs. Guidelines often recommend initiating annual DR screening at the time of type 2 diabetes diagnosis.[9] Our data strongly support the need for intensified vigilance in patients with long-standing disease. A patient with 15 years of diabetes, even with a fair HbA1c of 7.5%, may be at higher risk than a patient with 5 years of diabetes and a poor HbA1c of 9.0%. Every 1.0% increase in HbA1c significantly increases the odds of STDR.[16-20] Risk stratification models for referral and screening frequency should, therefore, heavily weight diabetes duration.

Limitations: The sample size, while sufficient for the primary analysis, limited the power for more complex subgroup analyses, such as comparing DME and PDR separately.

In conclusion, this analysis demonstrates that the duration of diabetes is the paramount independent risk factor for sight-threatening diabetic retinopathy. The relentless accumulation of microvascular damage over time appears to be the central pathological process. These results reinforce the critical importance of long-term, holistic diabetes management and advocate for risk-based screening protocols that prioritize patients with long-standing disease, ensuring timely detection and intervention to prevent blindness.

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