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Study on Risk Factors Associated with Severity of Diabetic Retinopathy in Type-2 Diabetic Patients, Attending a Tertiary Care Centre in Kerala

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ABSTRACT

Introduction: Diabetic retinopathy (DR) is a significant public health concern affecting individuals with diabetes mellitus (DM). Despite treatment advances, a substantial proportion of patients do not respond adequately. This study investigates risk factors associated with the progression of non-proliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR) in type-2 diabetes patients.

Methods: A retrospective case-control study was conducted on diabetic patients older than 40 years with at least 5 years of Type-2 Diabetes Mellitus history, attending ophthalmology clinic in Government Medical College, Thrissur, a tertiary care hospital. Data from patients with retinal examination showing diabetic retinopathy were analyzed. Records with missing data were excluded. Patients with Proliferative Diabetic Retinopathy (n=153) were compared with those having Non- Proliferative Diabetic Retinopathy (n=230). Various risk factors were assessed using statistical analysis.

Results: Among the studied variables, sex, duration of diabetes, serum urea, serum creatinine, serum triglycerides, and chronic kidney disease were significantly different between Proliferative Diabetic Retinopathy and Non-Proliferative Diabetic Retinopathy patients. Binary logistic regression revealed that duration of diabetes (OR = 1.8, 95% CI = 1.1 - 2.39) and serum creatinine (OR =1.8, 95% CI = 1.1 - 2.39) independently influenced Proliferative Diabetic Retinopathy development.

Conclusion: This study highlights that longer diabetes duration and elevated serum creatinine levels independently increase the risk of Non-Proliferative Diabetic Retinopathy progressing to Proliferative Diabetic Retinopathy in type-2 diabetic patients. Other factors such as age, gender, hyperlipidemia, systemic hypertension, type of diabetic treatment, and history of ischemic heart disease did not show significant associations with disease progression. These findings emphasize the importance of close monitoring, early detection, and intervention in patients with Non- Proliferative Diabetic Retinopathy, particularly those with a longer diabetic history, to prevent Proliferative Diabetic Retinopathy development. Further research should explore the causal relationship between serum creatinine and diabetic retinopathy progression and evaluate the impact of renal disease management on disease outcomes.

Keywords: *Diabetic Retinopathy*, diabetes mellitus (DM), Type-2 Diabetes Mellitus (T2DM).

INTRODUCTION

Diabetic retinopathy (DR) is a sight-threatening retinal vascular pathology that occurs in individuals with diabetes mellitus (DM) and remains a significant global public health concern. It is estimated that approximately 17.6% of the population with diagnosed Type-2 Diabetes Mellitus (T2DM) attending tertiary care centers in India have DR. [1] DR is the leading cause of blindness in adults, affecting about 12% of individuals with type 1 and type-2 diabetes aged over 40. [2,3] The impact of

DR on visual function and quality of life is substantial, with bilateral disease causing the most significant decrease in the quality-of-life index, particularly in terms of general vision, general health, and mental well-being. [4,5] With the rising trend of prevalence in the population affected by diabetes mellitus, the burden of diabetic retinopathy is also expected to increase proportionately. [6] Despite the advances in treatment modalities, such as intravitreal vascular endothelial growth factor inhibitors, a substantial proportion of patients, up to 50%, fail to respond adequately to these therapies. [7] For patients with proliferative disease, laser photocoagulation remains the mainstay of treatment, but it is inherently destructive and has its limitations. [7] Therefore, it is imperative to focus on strategies aimed at preventing the progression of DR, as early detection and intervention play a crucial role in mitigating the impact of this disabling disease. Numerous empirical studies have been conducted to identify risk factors associated with the development and severity of DR. Comorbidities such as impaired renal function, uncontrolled T2DM, hypertension, and dyslipidemia have been shown to be prevalent among individuals with proliferative diabetic retinopathy. [8, 9] However, many of these studies did not specifically investigate factors associated with the progression of DR, as they did not segregate subjects based on the stage of diabetic retinopathy for comparison of risk factors among them.

To address this gap in the literature, the present study aims to investigate the significant association between various cardiac and renal risk factors, namely age, gender, duration of diabetes, history of ischemic heart disease, hypertension, serum levels of urea, creatinine, cholesterol, and triglycerides, and the progression of NPDR into PDR. Identifying modifiable risk factors associated with disease progression may offer opportunities for targeted interventions to retard the advancement of DR and preserve visual function and quality of life.

MATERIALS & METHODS

A retrospective case-control study was conducted in the ophthalmology outpatient clinic at the Government Medical College, Thrissur. Clinical records of 383 diabetic patients older than 40 years with at least 5 years of history of type-2 diabetes mellitus who had given prior consent to use their data for research purposes were analyzed. Their retinopathy status was categorized into proliferative and non-proliferative diabetic retinopathy using ETDRS criteria. Only records of patients with complete documentation of their retinal examination that showed features of diabetic retinopathy were included in the study. Therefore, the data collection was restricted by incompletely recorded examination and investigation results. Hence, those records with missing data were excluded.

The data of the included patients, mainly their age, gender, duration of diabetes, diabetic status, history of ischemic heart disease, hypertension, serum levels of urea, creatinine, cholesterol, and triglycerides, were accessed from their hospital records through proper channels, excluding any patient-identifiable information.

Records of 153 patients diagnosed with proliferative diabetic retinopathy (PDR) were age- and gender-matched with those of 230 patients with non-proliferative diabetic retinopathy (NPDR), who served as controls. Numerical variables were expressed as the mean and standard deviation. Categorical variables were expressed as frequency and percentage. The chi-square test was used to test the association of study variables with outcomes. Multiple-variable logistic regression analysis was done for the significant variables in bivariate analysis. The data was entered into MS Office Excel and analyzed by IBM SPSS version 25. The p-value of 0.05 is considered statistically significant.

RESULT

For the purpose of this study, 383 records of patients above 40 years of age with a minimum 5-year history of Type-2 diabetes mellitus who had visited the Ophthalmology Outpatient Clinic in Government Medical College Thrissur were analyzed. The study population had a mean age of 59.26 ± 7.40 years and included 209 males (54.6%) and 174 females (45.4%). Patients diagnosed with proliferative diabetic retinopathy (n = 153) were taken as cases, in contrast to patients with non-proliferative diabetic retinopathy, who were taken as controls (n = 230). Upon univariate analysis, sex, duration of diabetes, serum urea, serum creatinine, serum triglycerides, and the presence of chronic kidney disease were significantly different among patients with and without proliferative diabetic retinopathy. Whereas there was no significant difference in age, type of treatment for diabetes, presence of systemic hypertension, history of ischemic heart disease, or serum cholesterol between patients with and without PDR. The above result has been compiled in table-1.

Clinical Information	Non-Proliferative retinopathy in % (n= 230)	Proliferative Retinopathy in % (n= 153)	P- Value
Sex (male/female)	53.1/68.3	46.8/31.6	0.014
Age (>60 years)	46.0	45.8	0.712
Duration of Diabetes (>10 years)	57.8	75.8	0.002
Type of Treatment			0.092
Tablets	64.3	54.2	
Insulin	22.6	26.8	
Tablets + Insulin	13.1	19.0	
HTN (previously diagnosed)	38.2	39.2	0.635
CKD (previously diagnosed)	3.47	13.7	0.002
Serum Cholesterol (>200mg/dl)	43.9	51.6	0.301
Triglycerides (>150mg/dl)	40.0	48.4	0.035
Urea (>40mg/dl)	9.5	38.6	<0.001
Creatinine (>1.35 mg/dl)	22.6	63.4	<0.001
IHD	7.8	6.5	0.215

Table 1: Univariate analysis of the significance of various cardiovascular risk factors on proliferative and non-proliferative diabetic retinopathy.

Upon binary logistic regression analysis, the duration of diabetes (OR = 1.8, 95% CI = 1.1-2.39) and serum creatinine (OR = 1.8, 95% CI = 1.1-2.39) had independent effects on the development of PDR. This has been tabulated in table-2.

Other Particulars	p	Adj. OR	95% CI for adj OR
SEX	0.150	0.7	0.5 – 1.1
Duration of diabetes	0.014	1.8	1.1 – 2.39
CKD	0.870	1.1	0.4 – 2.9
S, Urea	0.145	1.7	0.8 – 3.6
S. Creatinine	<0.001	3.0	1.7 – 5.1

Table 2: Binary logistic regression model for analysing significant variables from univariate analysis.

DISCUSSION

In this retrospective case-control study, we investigated the association between various cardiac and renal risk factors and the progression of non-proliferative diabetic retinopathy (NPDR) into proliferative diabetic retinopathy (PDR) in patients with type-2 diabetes mellitus T2DM) attending a tertiary care center in Kerala, India.

Our findings revealed that two factors, namely, duration of diabetes and serum creatinine levels, were significantly associated with the progression of NPDR to PDR. Specifically, patients with a longer duration of diabetes were found to be at higher risk of developing PDR. This finding aligns with previous studies that have linked the duration of diabetes to the prevalence of diabetic retinopathy in general. [10,11]

However, our study uniquely focused on assessing the duration of diabetes as a risk factor for progression from NPDR to PDR by comparing the two groups separately. This approach provides valuable insights into the longitudinal course of the disease and emphasizes the importance of closely monitoring patients with NPDR, especially those with a longer diabetic history, to detect and prevent the progression into PDR.

Furthermore, we observed that elevated serum creatinine levels were independently associated with the development of PDR. This finding is consistent with the studies that show impaired renal function as a risk factor for the progression of diabetic retinopathy. [10,11] While the exact mechanism underlying this association remains to be elucidated, it is likely that renal dysfunction contributes to systemic, metabolic, and inflammatory changes that exacerbate retinal vascular damage in diabetic patients. [12] Future research should be designed to investigate the causal relationship between elevated serum creatinine and the progression of diabetic retinopathy. Moreover, exploring whether adequate management of renal disease can delay the progression of diabetic retinopathy would be of significant clinical relevance. On the other hand, our study did not find a significant association between age, gender, hyperlipidemia, systemic hypertension, type of diabetic treatment, and history of ischemic heart disease with the progression of NPDR to PDR. These results are in line with some previous studies that also failed to establish a strong causal relationship between these factors and the progression of diabetic retinopathy. [13] However, it is important to note that these risk factors are still relevant concerning the overall development and severity of diabetic retinopathy. For instance, systemic hypertension has been linked to the prevalence of diabetic retinopathy in general, and elevated total cholesterol has been associated with the progression of diabetic retinopathy in some studies. [10,11] Therefore, while these factors may not directly influence the transition from NPDR to PDR, they remain crucial in the overall management and prevention of diabetic retinopathy.

The strengths of our study lie in its robust design as a retrospective case-control study, including a substantial number of patients with well-characterized retinopathy status. The use of stringent ETDRS criteria for categorizing retinopathy status added to the reliability of our findings. Additionally, we meticulously collected data on various cardiac and renal risk factors, enabling us to comprehensively analyze their associations with the disease progression. However, some limitations should be acknowledged. Firstly, the study's retrospective nature may have introduced inherent biases, such as selection bias and incomplete data. Prospective cohort studies could provide more robust evidence on causality and disease progression. Secondly, while we focused on the role of cardiac and renal risk factors, other factors such as smoking, and genetic predisposition could also play a role in diabetic retinopathy progression and should be considered in future investigations.

In conclusion, this study contributes valuable insights into the risk factors associated with the progression of diabetic retinopathy in patients with type-2 diabetes. The findings underscore the importance of close ophthalmic and renal function monitoring in patients with non-proliferative diabetic retinopathy, particularly those with a longer duration of diabetes, to detect and prevent the progression to proliferative disease. Early detection and intervention may help in delaying the advancement of this disabling complication and improving patients & quality of life. Future research should focus on exploring the mechanisms underlying the association between elevated serum creatinine and diabetic retinopathy progression and investigating the potential benefits of renal disease management in retinopathy outcomes.

CONCLUSION

This study provides valuable insights into the risk factors associated with the progression of diabetic retinopathy in patients with type-2 diabetes. The results indicate that a longer duration of diabetes and elevated serum creatinine levels are independent risk factors for the progression from non-proliferative diabetic retinopathy to proliferative diabetic retinopathy. However, other factors such as age, gender, hyperlipidemia, systemic hypertension, type of diabetic treatment, and history of ischemic heart disease did not show significant associations with disease progression. These findings highlight the importance of close ophthalmic and renal function monitoring in patients with non-proliferative diabetic retinopathy, especially those with a longer diabetic history, to detect and prevent the progression to proliferative disease. Future research should explore the causal relationship between elevated serum creatinine and the progression of diabetic retinopathy and assess the impact of adequate renal disease management on delaying disease progression.

Declaration by Authors

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