



ASSOCIATION BETWEEN DURATION OF DIABETES AND SEVERITY OF DIABETIC RETINOPATHY IN A CENTRAL INDIAN POPULATION

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ABSTRACT

Background: Diabetic retinopathy (DR) is one of the leading causes of preventable blindness and visual impairment in adults around the world due to the rising prevalence of type 2 diabetes mellitus (T2DM). The duration of diabetes is a known, non-modifiable risk factor for the development of microvascular complications. However, there is a dire need for regional epidemiological data mapping that associates the exact duration of diabetes with the graded severity of DR. This will help in designing localised public health and screening policies. The aim of this study was to evaluate the relationship between duration of diabetes and severity of diabetic retinopathy in a unique population of Central India.

Methods: A hospital-based, cross-sectional, observational study was conducted for a period of six months at a tertiary care center in Central India. The study enrolled 75 adult patients with previously diagnosed type 2 diabetes mellitus (T2DM). Dilated ophthalmic examinations included slit-lamp biomicroscopy and binocular indirect ophthalmoscopy. Diabetic retinopathy was graded according to Early Treatment Diabetic Retinopathy Study (ETDRS) classification criteria. The obtained data such as age, sex, duration of diabetes, glycaemic control and systemic comorbidities were subjected to statistical analysis using descriptive statistics, Chi-square test and correlational analyses.

Results: Overall prevalence of DR was 58.7% (n=44) of 75 subjects evaluated. A statistically significant positive correlation was found between the duration of diabetes and the severity of DR. The prevalence of DR was low (22.2%) in patients with <5 years of diabetes duration and was characterised mainly by mild non-proliferative changes. Conversely, 91.7% of patients with diabetes for more than 15 years had retinal complications and severe NPDR and PDR were found in 41.7% of this group within this time. Synergistic effects on severity were observed for other variables, e.g., coexisting hypertension and increased HbA1c levels.

Conclusion: Chronicity of diabetes mellitus is the major determinant of the onset and progressive severity of diabetic retinopathy in Central Indian population. The exponential rise in vision threatening DR after a decade of disease duration emphasises the critical need for rigorous annual

retinal screening in a protocol driven manner for all diabetic patients to detect early and intervene timely to prevent irreversible ocular morbidity.

Key words: Diabetic retinopathy, diabetes duration, non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, Central India, microvascular complications.

INTRODUCTION

Diabetes mellitus is among the most serious public health emergencies in the 21st century worldwide. Metabolic syndrome is defined as chronic hyperglycaemia resulting from defects in insulin secretion or insulin action, or both. Sustained systemic hyperglycemia predisposes patients to a variety of macrovascular and microvascular complications. Among the microvascular complications, diabetic retinopathy (DR) is the most specific and universally prevalent ocular complication and a leading cause of preventable blindness in working-age adults worldwide [1]. The worldwide prevalence of DR among people with diabetes is estimated to be approximately 34.6% and vision-threatening DR affects almost 10.2% of the diabetic population [2].

The epidemiological situation of diabetes in India is very alarming. India, which is often referred to as the “diabetes capital of the world,” has a rising diabetic population due to rapid urbanisation, sedentary lifestyle and genetic predisposition [3]. The collateral burden of DR is increasing in proportion to the increasing incidence of type 2 diabetes mellitus (T2DM). The national prevalence of DR has been reported to be in the range of 18–25%, but the specific prevalence is known to vary widely with geographical location, degree of urbanisation, and the demographic profile of the cohort studied [4]. The pathophysiology of DR is closely related to chronic sustained hyperglycemia that leads to a cascade of biochemical abnormalities such as activation of the polyol pathway, increased formation of advanced glycation end-products (AGEs), activation of protein kinase C (PKC), and upregulation of the hexosamine pathway [5]. These interconnected pathways result in severe oxidative stress, endothelial dysfunction, pericyte apoptosis and eventual disruption of the inner blood-retinal barrier [6]. Hence, retinal ischaemia occurs with subsequent up-regulation of vascular endothelial growth factor (VEGF) and development of pathological neovascularisation, the hallmark of proliferative diabetic retinopathy (PDR) [7]. The duration of diabetes is recognised in the global literature as the most important, independent, and non-modifiable predictor for both the incidence and progression of DR [8], given the progressive nature of these biochemical insults. Landmark studies such as the United Kingdom Prospective Diabetes Study (UKPDS) and the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) have clearly shown that the incidence of DR increases as a direct function of the duration of the metabolic disease [9]. However, the specific time point at which mild retinal changes progress to vision-threatening severe non-proliferative diabetic retinopathy (NPDR) or PDR may vary widely among different ethnic and regional populations due to differences in genetic constitution, local dietary habits and pre-existing systemic health factors [10]. Central India is a separate demographic and socio-economic zone. Though the importance of chronicity of disease in the natural history of DR is well established, localised tertiary level clinical data explaining the exact relation of specific duration of diabetes with the graded severity of retinopathy among the Central Indian population is clearly scanty. Knowing this region-specific timeline is key to optimising public health guidelines, resource allocation, and timing of a targeted screening protocol. Hence the main aim of this study was to determine the exact correlation of duration of previously diagnosed type 2 diabetes mellitus to severity of diabetic retinopathy in a tertiary care setting in Central India.

MATERIAL AND METHODS

Study Design and Study Period

A meticulous cross sectional observational analytical study was meticulously planned and executed in the Department of Ophthalmology of a well recognised tertiary care medical college and hospital of Central India. Six months of continuous collection of clinical data was performed.

Study Population and Sample Size

The study group comprised 75 adult patients (N = 75) who presented to the ophthalmic outpatient department (OPD) with a documented history of type 2 diabetes mellitus. All eligible patients who met the stringent inclusion and exclusion criteria within the stipulated six month study window were purposively sampled to determine the sample size.

Inclusion and Exclusion Criteria

Inclusion criteria required participants to be adults (18 years or older) with a confirmed diagnosis of T2DM, capable of giving informed consent, and cooperative for a full ophthalmic examination. Confounding pathologies were eliminated with stringent exclusion criteria. Patients with dense media opacities (e.g., mature cataract, severe corneal scarring) that precluded an unobstructed high-definition view of the retinal fundus were excluded. Also, patients with a known history of previous retinal interventions such as panretinal photocoagulation (PRP) laser therapy, focal/grid macular laser, intravitreal anti-VEGF injections or pars plana vitrectomy were excluded as such treatments significantly alter the natural course and grading of the retinopathy. Patients with coexisting non-diabetic retinal vascular disease e.g. central retinal vein occlusion, hypertensive retinopathy grade III/IV or severe macular degeneration were also excluded from the final analysis.

Clinical Evaluation and Data Collection

Demographic and clinical data were collected using a structured, pre-tested and standardised clinical proforma. Detailed history taking for chronological duration of diabetes (from the exact date of diagnosis by a medical professional to the date of the current ophthalmic examination), type of anti-diabetic treatments (oral hypoglycemic agents, insulin or both) and presence of comorbid systemic conditions, especially hypertension. Recent biochemical parameters including glycosylated haemoglobin (HbA1c) values checked over the past four weeks were recorded.

A detailed ophthalmic assessment started with the measurement of best-corrected visual acuity (BCVA) by a standard Snellen chart. Intraocular pressure (IOP) was measured by Goldmann applanation tonometry to rule out coexisting glaucoma. Careful slit-lamp biomicroscope was done for anterior segment evaluation. Then pupils were dilated with Tropicamide 1% and Phenylephrine 2.5% eye drops. The main part of the evaluation was a careful stereoscopic examination of the posterior segment. This was mainly done by slit-lamp biomicroscopy with a +90 Diopter Volk lens to evaluate the macula and optic nerve head stereoscopically. In addition, the peripheral retina was examined for ischaemic changes and neovascularisation by binocular indirect ophthalmoscopy (BIO) with a +20 Diopter lens.

Grading of Diabetic Retinopathy

The clinical diagnosis and subsequent stratification of DR severity were systematically graded based on the globally validated Early Treatment Diabetic Retinopathy Study (ETDRS) scale [11]. The grading was categorized into the following distinct clinical stages:

- 1.No Diabetic Retinopathy: Absence of any distinct diabetic microvascular abnormalities.
- 2.Mild Non-Proliferative Diabetic Retinopathy (NPDR): Presence of microaneurysms only.
- 3.Moderate NPDR: More than just microaneurysms, but less than severe NPDR (presence of dot and blot hemorrhages, hard exudates, and cotton wool spots).
- 4.Severe NPDR: Characterized by any one of the following criteria (the 4-2-1 rule): severe intraretinal hemorrhages and microaneurysms in all four quadrants, venous beading in two or more quadrants, or prominent intraretinal microvascular abnormalities (IRMA) in at least one quadrant, without signs of proliferation.
- 5.Proliferative Diabetic Retinopathy (PDR): Defined by the presence of neovascularization

of the disc (NVD), neovascularization elsewhere (NVE), pre-retinal hemorrhage, or vitreous hemorrhage. (Note: For analytical purposes in the data presentation, Severe NPDR and PDR were aggregated into a single cohort denoting "Vision-Threatening/Advanced DR"). Where bilateral DR was present but asymmetrical, the grade of the eye with the more advanced disease severity was utilized for the patient's overall categorical classification.

Statistical Analysis

Raw clinical data were gathered and put into tables in Microsoft Excel and rigorous statistical analysis was applied. Continuous variables (e.g. age, HbA1c) were reported as mean and standard deviation (SD). Categorical variables (gender, duration brackets and severity grades) were described as absolute frequencies and percentages. The statistical significance of the association between categorical variables, such as the dependence of DR severity on the duration of diabetes and other systemic risk factors, was determined using the chi-square (χ^2) test. Statistical significance was defined as $p < 0.05$.

RESULTS

The clinical study included a total cohort of 75 type 2 diabetes mellitus patients. A detailed description of the baseline sociodemographic and clinical characteristics of the study population is provided in Table 1. The mean age of participants was 54.2 years (SD $\pm$ 8.5) indicating mainly middle-aged to elderly population as is characteristic of T2DM complications. The cohort was predominantly male: 56.0% (n=42) males and 44.0% (n=33) females. The duration of diabetes in the subjects was different; the largest group of patients (33.3%, n=25) had a chronicity of disease between 5 and 10 years. The cohort's mean HbA1c was 8.2% (SD $\pm$ 1.4) indicating generally suboptimal systemic glycaemic and vascular parameter control in the referred population. Essential hypertension was a common comorbidity, found in 45.3% (n=34) of the subjects investigated.

Table 1: Baseline Sociodemographic and Clinical Characteristics of the Study Population (N = 75)

Clinical Characteristic	Value / Distribution	Percentage (%)
Age (years), Mean $\pm$ SD	54.2 $\pm$ 8.5	-
Gender		
- Male	42	56.0 %
- Female	33	44.0 %
Duration of Diabetes (years)		
- < 5 years	18	24.0 %
- 5–10 years	25	33.3 %
- 11–15 years	20	26.7 %
- > 15 years	12	16.0 %
Mean Glycosylated Hemoglobin (HbA1c %)	8.2 $\pm$ 1.4	-
Co-morbid Systemic Hypertension		
- Present	34	45.3 %
- Absent	41	54.7 %

The overall prevalence and diagnostic stratification of diabetic retinopathy for the 75 patients is shown in Table 2. Clinical examination revealed that 41.3% (n=31) patients had no visible signs of diabetic retinopathy. Thus, the overall prevalence of DR in the present Central Indian tertiary care

cohort was found to be 58.7% (n=44). When stratified for severity as per ETDRS classification, Mild NPDR was the commonest sub-type and represented 25.3% of the total cohort. However, vision-threatening advanced stages of the disease (Severe NPDR and PDR) were found in a considerable 13.3% of the total patient population, a high-risk group requiring urgent intervention.

Table 2: Overall Prevalence and Stratification of Diabetic Retinopathy (N = 75)

Grade of Diabetic Retinopathy	Number of Patients (n)	Percentage of Total Cohort (%)
No Diabetic Retinopathy (No DR)	31	41.3 %
Any Diabetic Retinopathy (Total DR)	44	58.7 %
- Mild NPDR	19	25.3 %
- Moderate NPDR	15	20.0 %
- Severe NPDR / PDR	10	13.3 %

Table 3 shows the categorical severity of DR based on the duration of diabetes and is the main result of the analysis conducted in this study. The data define a significant linear positive correlation between the chronicity of the metabolic disorder and the aggravation of the retinal microvascular pathology. Most of the patients (77.8%, n=14) diagnosed with diabetes for <5 years had no signs of DR in their pristine retinas whereas a small minority (22.2%) had mild/moderate changes and none (0.0%) had Severe NPDR or PDR. Conversely, the clinical picture deteriorated rapidly as the disease process advanced. In the group with diabetes for more than 15 years, any DR prevalence increased to a critical 91.7%. Moreover, the severity profile shifted significantly toward advanced stages of the disease; in this >15 year subgroup, an astonishing 41.7% (n=5) of patients presented with Severe NPDR or full blown PDR.

Table 3: Association Between Duration of Diabetes and Severity of Diabetic Retinopathy

Duration of Diabetes	No DR (n, %)	Mild NPDR (n, %)	Moderate NPDR (n, %)	Severe NPDR / PDR (n, %)	Total (N)
< 5 years	14 (77.8%)	3 (16.7%)	1 (5.5%)	0 (0.0%)	18
5–10 years	11 (44.0%)	8 (32.0%)	4 (16.0%)	2 (8.0%)	25
11–15 years	5 (25.0%)	6 (30.0%)	6 (30.0%)	3 (15.0%)	20
> 15 years	1 (8.3%)	2 (16.7%)	4 (33.3%)	5 (41.7%)	12
Total	31	19	15	10	75

Duration was the main variable of interest but the synergistic effect of glycemic control on DR severity was also analysed (Table 4). Patients were stratified according to their HbA1c level. The data showed that tight glycaemic control (HbA1c < 7.0%) was highly protective with 81.3% of these patients having no DR. However, in patients with severely uncontrolled diabetes (HbA1c > 8.5%), only 17.2% were free from retinopathy and incidence of Moderate to Severe NPDR/PDR was significantly high. Thus, the risk of retinal neovascularisation is exponentially increased by

increased duration of diabetes along with poor glycaemic control.

Table 4: Association of Glycemic Control (HbA1c Levels) with Diabetic Retinopathy Severity

Glycemic Status (HbA1c)	No DR (n, %)	Mild NPDR (n, %)	Moderate NPDR (n, %)	Severe NPDR / PDR (n, %)	Total (N)
Optimal (< 7.0 %)	13 (81.3%)	2 (12.5%)	1 (6.2%)	0 (0.0%)	16
Suboptimal (7.0 - 8.5 %)	13 (43.3%)	10 (33.3%)	5 (16.7%)	2 (6.7%)	30
Poor (> 8.5 %)	5 (17.2%)	7 (24.1%)	9 (31.0%)	8 (27.6%)	29

Table 5 shows the effect of comorbid systemic hypertension on presentation of DR. The prevalence of overall DR was significantly higher in patients with comorbid hypertension (70.6%) as compared to normotensive diabetic subjects (48.8%). Furthermore, the more advanced and vision-threatening forms of the disease (Severe NPDR/PDR) were disproportionately higher in the hypertensive cohort (20.6% vs 7.3%), highlighting the additive endothelial damage caused by the concurrent elevated systemic blood pressure over the course of the metabolic disease.

Table 5: Distribution of Diabetic Retinopathy According to Comorbid Systemic Hypertension

Hypertension Status	No DR (n, %)	Mild NPDR (n, %)	Moderate NPDR (n, %)	Severe NPDR / PDR (n, %)	Total (N)
Normotensive (n=41)	21 (51.2%)	12 (29.3%)	5 (12.2%)	3 (7.3%)	41
Hypertensive (n=34)	10 (29.4%)	7 (20.6%)	10 (29.4%)	7 (20.6%)	34

DISCUSSION

The present cross-sectional analytical study could establish the precise association of duration of type 2 diabetes mellitus with graded severity of diabetic retinopathy in a defined Central Indian population. The overall prevalence of DR in the study population was 58.7%. This prevalence is much higher than the rates reported in the larger population based Indian epidemiological surveys. For example, the seminal study by Raman et al. [12] reported an overall prevalence of DR of 18% in an urban Indian population, whereas more recent meta-analyses by Brar et al. [13] have quoted national prevalence figures in the range of 19% to 22%. The strikingly high prevalence found in this study (58.7%) is largely explained by the inherent selection bias of a tertiary care hospital setting, where patients are primarily referred because of symptomatic visual disturbances, advanced systemic disease or for a specific ocular intervention [14].

The main findings of this study are the clear and indisputable relationship between the duration of diabetes and the progressive damage to the microvasculature of the retina. We show empirically that the risk of developing retinopathy, and the risk of that retinopathy progressing to severe, vision-threatening stages, increase almost exponentially as the duration of disease goes beyond a decade. In particular, only 22.2% of patients with less than 5 years of disease duration had mild DR,

whereas a commanding 91.7% of patients surviving with diabetes for more than 15 years presented with clinically significant retinal complications. "Most worrisome, 41.7% of this very chronic group had Severe NPDR or PDR. This local evidence reflects and confirms the global scientific consensus on disease chronicity. Gelcho and Gari [15] also reported in a similar study in Ethiopia that the median time to DR onset was closely associated with the chronological duration of systemic hyperglycemia. Duration of the disease more than 10 years was the strongest independent predictor of retinopathy. Furthermore, Indian researchers, Jha et al. [16] observed that the severity of retinopathy and the collateral structural damage of the anterior segment including corneal endothelial deterioration worsens with the progression of diabetes duration and makes surgical intervention more difficult among chronic DR patients.

The pathophysiologic reason for this duration-dependent severity is the cumulative effect of metabolic memory and chronic microvascular stress. Prolonged hyperglycaemia over a 10 to 15 year period causes the gradual accumulation of Advanced Glycation End-products (AGEs) in the basement membranes of the retinal capillaries. This long-lasting biochemical insult results in an irreversible loss of pericytes, a structural failure that leads to capillary outpouching (microaneurysms), capillary occlusion, and crippling retinal ischaemia [17]. The ischaemic environment then causes massive upregulation of VEGF over time, shifting the retina from a non-proliferative state of stress (exudates and haemorrhages) to full-blown proliferative disease with fragile neovascular fronds [18]. Moreover, our study supported the synergistic role of poor glycaemic control and systemic hypertension in the accelerated duration-dependent severity of DR. Our results showed that patients with concomitant hypertension were more likely to have Severe NPDR and PDR. This is consistent with the findings of several recent trials, which state that the simple mechanical stress of increased intraluminal hydrostatic pressure worsens the endothelial leakage in vessels already damaged by chronic diabetic damage [19]. In a similar vein, the compounding effect of an elevated HbA1c ($> 8.5\%$) acts as an accelerator, effectively compressing the timeline needed for mild non-proliferative changes to devolve into blinding proliferative disease [20].

The localised study provides valuable insights, but it has limitations. The sample size ($n=75$) is statistically sufficient for correlational trends, but it is small, so the percentage distributions may not apply to Central India. Second, the hospital-based, cross-sectional design does not assume rigid temporal causality because we are looking at a snapshot of the population, not a cohort followed for 15 years. Third, since early T2DM is often asymptomatic and undetected, patients' recall and the date of formal diagnosis may underestimate the disease's biological duration.

Despite these limitations, this data's clinical recommendations are simple. The sharp rise in severe DR in patients aged 10 and 15 necessitates stratifying ophthalmological screening by disease age. The gold standard is annual screening, but central Indian public health policies must encourage biannual screening for diabetics over 10 years old, regardless of symptoms.

CONCLUSION

To conclude, this tertiary care study shows a strong, positive, and linear association between type 2 diabetes duration and diabetic retinopathy severity in Central Indians. The results show that while early-stage diabetes poses less immediate ocular risk, its chronicity drives retinal microvascular failure. The exponential increase in vision-threatening Severe NPDR and PDR after 15 years of disease shows that total metabolic insult over time is the final common pathway to irreversible diabetic vision loss. Regional health authorities must promote aggressive early glycaemic control and strict annual retinal screening to detect subclinical microvascular changes before they cause structural ocular pathology.

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