ORIGINAL ARTICLE

A Study to Assess the Prevalence, Risk Factors, and Role of Epicardial Fat Thickness in Prediction of Diabetic Retinopathy in Type 2 Diabetic Patients in a Tertiary Care Center in Western Uttar Pradesh

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Abstract

Introduction: Diabetic retinopathy (DR) is the most important risk factor causing blindness in diabetic individuals, and its risk progresses with increased disease duration. Epicardial fat thickness (EFT) is an emerging indicator of inflammation and metabolic derangement and has been proposed as a potential biomarker linked to the severity of DR. This study aims to assess the prevalence of DR, identify risk factors associated with DR, and evaluate the predictive role of EFT in detecting DR in subjects with type 2 diabetes mellitus (T2DM).

Methods: A cross-sectional observational study was conducted at LLRM Medical College, Meerut, from 2023 to 2024. The participants included 130 T2DM patients who were assessed clinically, radiologically, and biochemically. Demographic data, duration of diabetes, body mass index (BMI), HbA1c levels, and EFT were measured. The severity of DR was determined based on ophthalmic examination. Data were analyzed using Kruskal–Wallis and Chi-squared tests.

Results: In this study of 130 patients with T2DM, 64.61% ($n = 84$) had DR, including 33.84% ($n = 44$) with nonproliferative DR (NPDR) and 30.76% ($n = 40$) with proliferative DR (PDR), while 35.38% ($n = 46$) had no DR. Patients in the PDR group were older on average (60.5 ± 13.9 years), but age differences were not statistically significant ($p = 0.154$). The duration of diabetes was significantly longer in PDR patients (9.0 ± 3.01 years) compared with NPDR and non-DR groups ($p < 0.001$). BMI increased with DR severity, reaching 28.49 ± 2.07 kg/m^2 in the PDR group, in which 20% were obese and 72.5% were overweight. A higher waist–hip ratio (WHR) was significantly associated with more severe DR in males ($p < 0.001$) but not in females ($p = 0.099$). HbA1c levels increased with disease severity, from 6.1 ± 0.71% in non-DR to 8.6 ± 1.97% in PDR patients ($p < 0.001$). Similarly, EFT increased from 3.9 ± 0.47 mm in non-DR to 7.9 ± 1.09 mm in PDR ($p < 0.001$), suggesting EFT as a potential biomarker for DR severity. These findings highlight strong links between DR severity, poor glycemic control, obesity measures, and longer diabetes duration.

Conclusion: These findings suggest that in type 2 diabetes mellitus patients, EFT can serve as a significant marker for the severity of DR. It can be used as a noninvasive investigation to predict PDR. When considered alongside established risk factors such as BMI, HbA1c levels, and diabetes duration, EFT could enhance early identification of patients at risk, potentially helping to prevent advancement to the more severe proliferative stage (PDR). However, larger and more extensive studies are required to confirm these observations and strengthen their clinical relevance.

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Introduction

Diabetes mellitus (DM) is a longstanding metabolic disorder associated with high blood sugar due to ineffective insulin secretion or action.[1] It ranks among the top 10 causes of global mortality and morbidity, alongside cardiovascular and respiratory diseases and cancer. In 2021, an estimated 74 million adults in India had diabetes, and this number is assumed to reach 125 million by 2045, according to the International Diabetes Federation (IDF).[2]

Diabetic retinopathy (DR) is one of the main causes of preventable blindness in adults. People with diabetes are about 2.4 times more likely to experience vision loss compared with those who do not have the condition.[3,4] DR prevalence increases with diabetes duration, rising from 28.8% in those with <5 years of diabetes to 77.8% in those with >15 years.[5] DR is subdivided into nonproliferative (NPDR) and proliferative (PDR). While NPDR is often asymptomatic, PDR includes neovascularization and can cause severe vision loss.

Despite screening and treatments such as laser therapy, corticosteroids, and anti-VEGF agents, many patients respond poorly, indicating the need for better predictors so that timely treatment can be started and complications can be prevented.

Epicardial adipose tissue (EAT), fat surrounding the heart, has gained attention for its role in inflammation and metabolic syndrome. Epicardial fat is metabolically active and releases inflammatory cytokines such as IL-6 and TNF-α. These cytokines promote vascular injury and worsening of insulin resistance, which is responsible for DR.[6]

Recent studies show that epicardial fat thickness (EFT) is more significantly associated with DR severity in type 2 diabetes.[7] PDR patients had higher EFT, with values above 5.90 mm predicting PDR with 74% sensitivity and 61% specificity. EFT can be measured using echocardiography, cardiac CT, or MRI.[8]

Considering the limited existing research on the correlation between DR and EFT, this study focuses on finding the prevalence of DR and its associated risk factors. This study aims to assess the prevalence of DR, identify its risk factors, and explore the predictive potential of EFT in type 2 diabetes subjects at a tertiary care center in Western Uttar Pradesh.

Methods

This study was cross-sectional observational and was conducted in the departments of medicine, endocrinology, and ophthalmology at LLRM Medical College and SVBP Hospital, Meerut, during 2023–2024. It included young type 2 DM patients attending the

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OPD and IPD of medicine, endocrinology, and ophthalmology. Patients were evaluated clinically, radiologically, biochemically, pathologically, and via questionnaire. Ethical clearance was obtained from the institutional ethical committee with ref. no. SC-1/2025/2912, dated 23/04/2025.

The sample size for the study was determined using the standard formula: $n = 4\,pq/d^2$.

Where p is the prevalence of type 2 diabetes mellitus, taken as 7.2%,[9] and absolute error was taken as 5%. On calculation, the sample size came out to be 113, and a 10% nonresponse rate was added, making the sample size nearly 130.

Inclusion criteria included all confirmed T2DM patients (according to WHO criteria) aged over 18. Exclusion criteria included age below 18, severely ill patients, liver or thyroid disorders, electrolyte imbalances, inflammatory or infectious diseases, pregnancy, and those who did not give consent.

Anthropometric measurements included weight, height, waist circumference, and hip circumference. From these data, BMI and WHR were calculated. Demographic and lifestyle data were recorded, including age, sex, address, education, occupation, addictions, family history, diet, physical activity, and diabetes duration. General and systemic examinations were performed.

Investigations included hemogram (Hb, TLC, DLC, platelet count, RBC count, and indices), reticulocyte count, FBS, PPBS, HbA1c, lipid profile, LFT, KFT, echocardiography, chest X-ray, ECG, and fundus examination.

In this study, subjects with DR were classified based on ETDRS (Early Treatment Diabetic Retinopathy Study) guidelines as follows: (1) nondiabetic retinopathy (NDR), (2) nonproliferative diabetic retinopathy (NPDR), and (3) proliferative diabetic retinopathy (PDR). Further, NPDR was categorized into mild, moderate, severe, and very severe stages, while PDR was classified as early or high risk.

Epicardial fat thickness was assessed through echocardiography. EFT was determined in the parasternal long-axis view. It is the echo-free space observed between the visceral pericardium and the outer wall of the myocardium. EFT was measured during end systole, in which the ultrasound beam was aligned to the free wall of the right ventricle and kept perpendicular to the aortic annulus. The aortic annulus served as the reference point.

All collected data were organized into tables, and appropriate statistical tests, including the Kruskal–Wallis test, Chi-squared test, Fisher's exact test, and one-way ANOVA, were used for analysis. The results were compared across 3 patient groups: those without retinopathy (non-DR), those with NPDR, and those with PDR.

Results

In this study, all diabetic patients were divided on the basis of fundus examination into 3 groups. Group A contained patients who did not have any retinopathy. Group B included those having NPDR, and group C included those having PDR.

Figure 1 shows the prevalence of DR in type 2 diabetic patients in this study. Out of the 130 patients, 35.38% (n = 46) had no retinopathy, and 64.61% (n = 84) had DR. Of the 84 DR patients, 33.84% (n = 44) were in the NPDR group, and 30.76% (n = 40) were in the PDR group.

Table 1 shows the distribution of age. In the present study, out of 130 participants, 17.69% were under 40 years, 15.38% were in the 40–49 years age range, 20.77% were aged 50–59 years, and 46.15% were over 60 years. On analysis of age distribution in the 3 groups, the mean age was highest in the PDR group at 60.52 ± 13.9 years, followed by 58.52 ± 16.23 years in the NPDR group and 54.52 ± 14.45 years in the group without DR (non-DR). However, the differences in age among the groups were not statistically significant (p = 0.154).

Table 2 shows the association of DR with duration of type 2 diabetes mellitus (T2DM). In the study population, 23.08% of subjects had diabetes for <5 years, 61.54% for 5–9 years, and 15.38% for ≥10 years. The mean duration of diabetes was longest in the PDR group (9.0 ± 3.01 years), which was significantly higher than in the NPDR (6.0 ± 2.15 years) and non-DR (6.0 ± 1.93 years) groups (p < 0.001).

Subjects were divided based on BMI according to WHO criteria as normal (18.5–24.9), overweight (25–29.9), and obese (≥30).

Table 3 shows the association between DR, waist–hip ratio (WHR), and obesity (BMI). The mean BMI was highest in patients with PDR at 28.49 ± 2.07 kg/m^2, followed by those with NPDR at 27.0 ± 1.71 kg/m^2, and lowest in patients without DR at 26.0 ± 2.62 kg/m^2. When categorized by weight status, among patients without DR, 32.61% had normal weight, 67.39% were overweight, and none were obese.

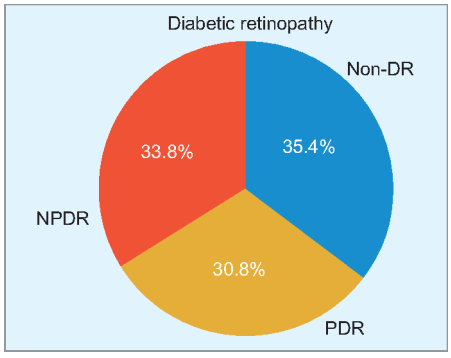

Fig. 1: Pie chart showing distribution of DR in our study

Table 1: Table showing the age distribution of subjects in our study

Parameter		*Group*	*Frequency*	*Percent*	*p-value*
Age-group		<40 years	23	17.69%	
		40–49 years	20	15.38%	
		50–59 years	27	20.77%	
		≥60 years	60	46.15%	
		Total	130	100%	
Age-group		Non-DR (n = 46)	NPDR (n = 44)	PDR (n = 40)	
	Mean (SD)	54.52 (±14.45)	58.52 (±16.23)	60.52 (±13.9)	H statistic: 3.746 p-value: 0.154[a]
	Median (IQR)	55.5 (44.5–64.0)	59.5 (42.5–76.0)	62.0 (50.0–75.25)	
	Min–max	29.0–76.0	34.0–76.0	34.0–76.0	

[a]Kruskal–Wallis test

Table 2: Table showing the association between DR and duration of T2DM

Parameter		*DR*			*Total*	*p-value*
		Non-DR (n = 46)	*NPDR (n = 44)*	*PDR (n = 40)*		
Duration of T2DM (years)	Mean (SD)	6.0 (±1.93)	6.0 (±2.15)	9.0 (±3.01)		H statistic: 25.991; *p*-value: <0.001[a]
	Median (IQR)	7.0 (4.0–8.0)	5.5 (4.0–8.0)	8.5 (6.75–11.25)		
	Min–max	2.0–8.0	4.0–11.0	5.0–14.0		
Duration of T2DM (years)	<5 years	13 (43.33%)	17 (56.67%)	0 (0%)	30 (23.08%)	$\chi^2 = 43.908$; *p* value: <0.001[b]
	5–9 years	33 (41.25%)	24 (30%)	23 (28.75%)	80 (61.54%)	
	≥10 years	0 (0%)	3 (15%)	17 (85%)	20 (15.38%)	

[a]Kruskal–Wallis test; [b]Chi-squared test

Table 3: Table showing the association of DR with obesity and waist-to-hip ratio

Parameter		*DR*			*Total*	*p-value*
		Non-DR (n = 46)	*NPDR (n = 44)*	*PDR (n = 40)*		
BMI (kg/m^2)	Mean (SD)	26.0 (±2.62)	27.0 (±1.71)	28.49 (±2.07)		H statistic: 21.571; *p*-value: <0.001[a]
	Median (IQR)	26.39 (24.23–28.22)	27.15 (25.6–28.51)	28.48 (26.98–29.86)		
	Min–max	21.34–29.95	23.93–29.64	23.6–31.91		
Obesity	Normal (18.5–24.9)	15 (32.61%)	9 (20.45%)	3 (7.5%)	27 (20.77%)	<0.001[a]
	Overweight (25–29.9)	31 (67.39%)	35 (79.55%)	29 (72.5%)	95 (73.08%)	
	Obese ≥30)	0 (0.0%)	0 (0.0%)	8 (20.0%)	8(6.15%)	
Waist–hip ratio						*p*-value
Male	Excellent (<0.85)	6 (23.08%)	0 (0.0%)	1 (5.26%)	7 (10.14%)	<0.001[a]
	Good (0.85–0.89)	5 (19.23%)	0 (0.0%)	1 (5.26%)	6 (8.7%)	
	Average (0.9–0.95)	1 (3.85%)	0 (0.0%)	2 (10.53%)	3 (4.35%)	
	At risk (≥0.96)	14 (53.85%)	24 (100.0%)	15 (78.95%)	53 (76.81%)	
	Total	26	24	19	69 (100%)	
Female	Excellent (<0.75)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.099[b]
	Good (0.75–0.79)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Average (0.8–0.85)	3 (15.0%)	0 (0.0%)	1 (4.76%)	4 (6.56%)	
	At risk (≥0.86)	17 (85.0%)	20 (100.0%)	20 (95.24%)	57 (93.44%)	
	Total	20	20	21	61 (100%)	

[a]Kruskal Wallis Test; [b]Fisher's Exact test

Table 4: Table showing the association between DR and HbA1c

Parameter		*DR*			*p-value*
		Non-DR (n = 46)	*NPDR (n = 44)*	*PDR (n = 40)*	
HbA1c (%)	Mean (SD)	6.1 (±0.71)	7.41 (±0.97)	8.6 (±1.97)	H statistic: 48.557; *p*-value: <0.001[a]
	Median (IQR)	6.15 (5.52–6.6)	7.3 (6.68–8.15)	8.65 (6.65–10.25)	
	Min–max	4.8–7.2	6.0–9.2	6.2–11.8	
HbA1c	<7%	41 (58.57%)	16 (22.86%)	13 (18.57%)	<0.001[b]
	7–7.9%	5 (20.83%)	14 (58.33%)	5 (20.83%)	
	8–8.9%	0 (0%)	10 (71.43%)	4 (28.57%)	

[a]Kruskal–Wallis test; [b]Fisher's exact test

Among NPDR patients, 20.45% had normal weight, 79.55% were overweight, and none were obese. In contrast, among those with PDR, only 7.5% had normal weight, 72.5% were overweight, and 20% were obese. These results highlight a clear trend showing that increasing BMI is associated with greater severity of DR.

On evaluation of the relationship between DR and WHR in males, among those with an excellent WHR (<0.85), 23.08% had no DR and 5.26% had PDR. In the good category (0.85–0.89), 19.23% had no DR and 5.26% had PDR. Among those with an average WHR (0.90–0.95), 3.85% had no DR and 10.53% had PDR. In the at-risk group (WHR ≥0.96), 53.85% had no DR, 100.00% had NPDR, and 78.95% had PDR, with $p < 0.001$, showing that male subjects with higher WHR had greater severity of DR.

In females, no subjects fell into the excellent or good WHR categories. Among those with an average ratio (0.80–0.85), 15% had no DR and 4.76% had PDR. In the at-risk group (WHR ≥0.86), 85.00% had no DR, 100.00% had NPDR, and 93.44% had PDR. However, the difference observed among female participants was not statistically significant ($p = 0.099$). These findings suggest a strong association between higher WHR and severity of DR in males but not in females.

Table 4 shows the association between DR and HbA1c. The mean HbA1c level was

Table 5: Table showing the association between DR and EFT

Parameter		*DR*			*p-value*
		Non-DR (n = 46)	*NPDR (n = 44)*	*PDR (n = 40)*	
EFT (mm)	Mean (SD)	3.9 (±0.47)	6.9 (±0.9)	7.9 (±1.09)	H statistic: 95.23; *p*-value: <0.001
	Median (IQR)	3.8 (3.5–4.5)	6.9 (6.2–7.8)	8.2 (6.9–9.0)	
	Min–max	3.2–4.5	5.4–8.1	6.1–9.0	
EFT	<4 mm	28 (100%)	0 (0%)	0 (0%)	<0.001[a]
	4–5.9 mm	18 (69.23%)	8 (30.77%)	0 (0%)	
	6–7.9 mm	0 (0%)	28 (60.87%)	18 (39.13%)	
	≥8 mm	0 (0%)	8 (26.67%)	22 (73.33%)	

[a]Fisher's exact test

highest in the PDR group at 8.6 ± 1.97%, followed by 7.41 ± 0.97% in the NPDR group and 6.1 ± 0.71% in the non-DR group, with $p < 0.001$. When classified by HbA1c levels, 58.57% ($n = 41$) of patients in the non-DR group had HbA1c <7%, while 22.86% ($n = 16$) in the NPDR group and 18.57% ($n = 13$) in the PDR group had HbA1c <7%. In the 7.0–7.9% HbA1c group, 20.83% ($n = 5$) had no DR, 58.33% ($n = 14$) had NPDR, and 20.83% ($n = 5$) had PDR. Among those with HbA1c between 8.0% and 8.9%, none were without DR, while 71.43% ($n = 10$) had NPDR and 28.57% ($n = 4$) had PDR. The *p*-value of <0.001 indicates a strong correlation between higher HbA1c levels and increased severity of DR.

Table 5 shows the association between DR and EFT. The EFT was highest in the PDR group at 7.9 ± 1.09 mm, followed by 6.9 ± 0.9 mm in the NPDR group and 3.9 ± 0.47 mm in the non-DR group, with a statistically significant difference ($p < 0.001$). When categorized by EFT, among individuals with EFT <4 mm, almost all patients (100%) did not have DR. In the 4.0–5.9 mm category, 69.23% ($n = 18$) did not have DR, 30.77% ($n = 8$) had NPDR, and none had PDR. For those with EFT between 6.0 and 7.9 mm, none were without DR, while 60.87% ($n = 28$) had NPDR and 39.13% ($n = 18$) had PDR. In the ≥8 mm category, none were without DR, 26.67% ($n = 8$) had NPDR, and 73.33% ($n = 22$) had PDR, with $p < 0.001$, indicating a strong correlation between higher EFT and increased severity of DR.

Discussion

In coming years, it is expected that India will become the new capital of diabetes mellitus patients. This will definitely affect the global health burden of diabetes. In diabetic patients, the major challenge in treatment is the prevention of diabetic complications. Among its many complications, DR remains a major contributing factor to avoidable blindness and is closely related to the duration of the disease. In recent years, obesity, especially the accumulation of central and visceral fat such as epicardial adipose tissue (EAT), has been linked to factors responsible for the onset and progression of DR, likely due to its involvement in systemic inflammation and endothelial dysfunction.

In this study, the prevalence of NDR, NPDR, and DR was relatively similar. This contrasts with findings from several other studies, where NPDR is typically reported to be more common than PDR in individuals with T2DM. A large meta-analysis in Asia reported an overall DR prevalence of 21.7%, with NPDR at 19.9% and PDR at 2.3% among T2DM patients.[10] Another systematic review covering 2.6 million patients across Asia found DR in 28%, with NPDR in 27% and PDR in 6%.[11]

In this study, age did not show any significant association among the 3 groups, with similar mean ages and a similar proportion of participants aged 60 years or older. The association between age and DR remains inconclusive. While Kahn and Bradley[12] also reported similar findings showing a nonsignificant relationship between age and DR in patients with a duration of diabetes of >10 years, Chatziralli et al.[13] reported a positive correlation ($r = 0.4869$, $p < 0.0001$). These variations may be due to differences in study design, diagnostic methods, population characteristics, geographic regions, and confounding factors such as duration of diabetes, glycemic control, and access to health care services.

Gender also did not significantly impact DR, with no major differences between males and females in this study. Evidence regarding gender as a risk factor for DR is inconsistent. Kajiwara et al.[14] observed a higher incidence of retinopathy in females (76.1 vs 51.6 per 1,000 person-years). Conversely, Cherchi et al.[15] found a higher prevalence in males (22.0 vs 19.3%, $p < 0.0001$), while Ozawa et al.[16] showed no significant difference based on gender.

The duration of diabetes showed a positive correlation with DR severity. Patients diagnosed with PDR had a notably longer history of diabetes compared with those with NPDR or no retinopathy. There is strong consensus that longer diabetes duration significantly increases DR risk. Voigt et al.[17] demonstrated a rising DR prevalence with longer diabetes duration, reaching 63% at 30 years. Jerneld and Algvere[18] found duration to be the only significant predictor in multivariate analysis ($p < 0.001$). Raman et al.[19] reported an odds ratio of 6.43 (95% CI, 3.18–12.90) for DR in patients with diabetes >15 years compared with <15 years. These findings imply that duration of diabetes is a critical factor in the progression of DR. Therefore, annual screening for DR is essential, particularly for individuals with a longer duration of diabetes. Early detection through regular eye examinations can help identify retinopathy in its initial stages, allowing timely intervention and significantly improving patient outcomes.

In this study, body mass index (BMI) showed a positive correlation with DR severity, with higher BMI observed in PDR patients. Studies have shown conflicting results regarding the role of obesity in DR. Raman et al.[20] found a higher DR prevalence in individuals with abdominal obesity (26.35 vs 6.08%) and significant associations with increased waist–hip ratio (OR 1.48) and abdominal obesity (OR 2.02). However, other studies have reported an inverse association. Sabanayagam et al.[21] found lower DR odds in obese patients (OR 0.74; 95% CI, 0.59–0.91), and Rooney et al.[22] similarly reported lower odds for overweight and obese individuals compared with those of normal weight. These discrepancies may be due to differences in obesity definitions and measurement methods, variations in study populations such as age, ethnicity, and duration of diabetes, and confounding factors including medications and comorbid illnesses. These findings imply that, in addition to standard treatment, weight management is important. Furthermore, overweight or obese diabetic individuals should undergo more stringent ophthalmological screening for DR.

Waist–hip ratio (WHR) was also positively correlated with DR severity in males, with higher WHR corresponding to more severe DR. The association between central obesity and DR is well documented, although the effect in females was not significant, possibly due to hormonal differences. Fu et al.[23] reported significantly higher WHR values in subjects with DR compared with non-DR. Similarly, Zhang et al.[24] showed that subjects with higher WHR had 3 times higher likelihood of DR compared with those in the lower WHR group, with an odds ratio of 3.327 (95% CI, 2.386–4.638). The discrepancy between males and females may be attributed to hormonal differences. The significant association between high WHR and DR severity in males highlights the importance of measuring and managing abdominal obesity in addition to standard treatment.

HbA1c values showed a strong correlation with DR severity, with more advanced stages of DR observed in patients with higher HbA1c levels. This emphasizes the importance of maintaining good glycemic control to prevent DR progression. These findings indicate that glycemic control is of utmost importance in preventing the progression of DR. Yun[25] demonstrated a significantly increased DR risk in patients in the highest HbA1c quartile (OR 3.46; 95% CI, 1.90–6.30). The DCCT trial[26] demonstrated a 54% reduction in DR incidence and a 76% reduction in progression with intensive glycemic control.

Epicardial fat thickness showed a positive correlation, with higher values observed in patients with DR. EFT acts as a predictive biomarker for DR. Abide et al.[8] reported a positive correlation with PDR ($r = 0.394$, $p < 0.001$) and an independent association on regression analysis (OR 1.643; 95% CI, 1.206–2.237). Similarly, Gameli et al.[27] found elevated EFT in patients with DR and noted its predictive value for NPDR.

Conclusion

This study highlights the important factors that affect DR severity in subjects with T2DM, notably longer duration of the disease, increased body mass index (BMI), and elevated HbA1c levels. These findings emphasize the need for comprehensive risk assessment in diabetic care. Importantly, this study highlights the importance of 2 novel biomarkers that are also associated with DR, increased EFT and increased monocyte/HDL ratio. These novel biomarkers may aid in early detection of retinopathy cases, leading to improved patient outcomes. However, more extensive studies are necessary to substantiate these conclusions.

Limitations

This study had several limitations. Its cross-sectional observational study design, with a sample size on the relatively smaller side, limits the strength of the inferences drawn. Additionally, the study was single centric and did not include potential confounding factors. The use of a single-time glycemic measurement may not reflect long-term glycemic control, further limiting the generalizability of the findings to broader populations.

Recommendations

Future research should focus on large, multicenter, longitudinal studies and risk factor modification. High-resolution data from continuous glucose monitoring and the study of novel biomarkers are recommended. Interventional studies should also evaluate the impact of early risk factor modification on DR progression across diverse populations.

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