International Journal of Advances in Medicine
Sharma P et al. Int J Adv Med. 2025 Nov;12(6):558-562
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20253348

Original Research Article

Assessing the risk of heart failure in patients with diabetic retinopathy with type 2 diabetes mellitus

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Received: 17 June 2025
Revised: 22 July 2025
Accepted: 15 September 2025

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with both microvascular and macrovascular complications, notably diabetic retinopathy (DR) and heart failure (HF), respectively. While DR is a well-established marker of retinal microangiopathy, emerging evidence suggests it may also reflect systemic vascular pathology. However, data on this association in the Indian population remains limited.
Methods: A hospital-based cross-sectional observational study was conducted at GSVMMC, Kanpur, between August 2023 and February 2025. Ninety-two adults with T2DM were enrolled and assessed for DR using fundoscopic examination and graded from 0 to 3. Heart failure was diagnosed and classified via echocardiography into HFpEF, HFmrEF, and HFrEF. Biochemical markers, including HbA1c and NT-proBNP, were evaluated. Statistical analysis included Chi-square tests and ANOVA using statistical package for the social sciences (SPSS) v20.
Results: Among the 92 patients, 73 (79.34%) had some form of heart failure, and 74 (80.43%) had DR. A significant association was found between DR and HF (p=0.001). The prevalence of HFrEF increased with DR severity from 10% in grade 0 to 35% in grade 3 DR (p=0.045). Additionally, poor glycemic control and higher body mass index (BMI) were common in patients with more severe DR and HF.
Conclusion: DR is significantly associated with both the presence and severity of HF in T2DM patients. Retinal examination may serve as a practical, non-invasive tool for early cardiovascular risk stratification. These findings support integrated screening strategies in diabetic care.

Keywords: Type 2 diabetes mellitus, Diabetic retinopathy, Heart failure, HFrEF, Cardiovascular risk, Microvascular complications

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global health concern, with its complications contributing significantly to morbidity and mortality. Among these, diabetic retinopathy (DR) a microvascular complication and heart failure (HF) a macrovascular complication are particularly debilitating. While DR is a leading cause of blindness, HF remains a critical cardiovascular outcome in diabetic patients, often resulting in poor prognosis and increased healthcare burden. Emerging evidence suggests that DR may serve as an early marker for systemic vascular dysfunction, including cardiovascular diseases such as HF, due to shared pathological mechanisms like endothelial dysfunction, chronic inflammation, and oxidative stress.[1,2]

The pathophysiological link between DR and HF lies in their common metabolic and vascular pathways. Chronic hyperglycemia in T2DM leads to advanced glycation end-products (AGEs), oxidative stress, and activation of the renin-angiotensin-aldosterone system (RAAS), all of which contribute to both retinal microvascular damage and myocardial dysfunction.[3] Studies indicate that patients with DR have a 2-3 times higher risk of developing HF, particularly HF with reduced ejection fraction (HFrEF), compared to those without DR.[4]

However, most existing research is derived from Western populations, with limited data from India, where the dual burden of diabetes and cardiovascular disease is rapidly escalating.

Despite advancements in diabetes management, early detection of HF risk in T2DM patients remains challenging. Current risk prediction models primarily rely on traditional factors like hypertension and dyslipidemia, often overlooking microvascular indicators such as DR. Given that retinal examination is a simple, non-invasive tool, integrating DR screening into HF risk assessment could enhance early intervention strategies, especially in resource-limited settings.

Objectives

This objectives of the study were to assess the risk of HF in T2DM patients with DR compared to those without DR and to evaluate the association between DR severity and HF subtypes (HFpEF, HFmrEF, and HFrEF).

METHODS

Study design

This was a hospital-based, cross-sectional observational study conducted to assess the association between DR and HF in patients with T2DM. The study design allowed for simultaneous evaluation of DR severity and HF subtypes, providing a snapshot of their relationship.

Setting

The study was conducted at the Department of General Medicine, Ganesh Shankar Vidyarthi Memorial Medical College (GSVMMC), Kanpur, Uttar Pradesh, India, from August 2023 to February 2025. Participants were recruited from both outpatient (OPD) and inpatient (IPD) departments to ensure a representative sample.

Participants

A total of 92 patients with T2DM were recruited of age >34 years with confirmed T2DM by WHO criteria. Excluding those with stroke, coronary artery disease, other retinopathies, CKD or alcoholism.

Variables

The primary variable of interest was the presence of HF (classified as HFpEF, HFmrEF, or HFrEF) in patients with DR, while secondary variables included DR severity (grades 0–3), NYHA functional class (I–IV) and biochemical markers (HbA1c, NT-proBNP).

Data source/measurements

Data were collected through structured interviews, clinical examination and fundoscopy, medical records, and biochemical measurements, including fasting blood sugars, HbA1c, Nt-Pro BNP and routine investigations, confirmed and severity grading of heart failure is done by 2D echo for ejection fraction.

Bias

To minimize bias, strict inclusion and exclusion criteria were applied, and random sampling methods were utilized to ensure a representative sample of the population.

Study size

The sample size was calculated based on the estimated prevalence of diabetic retinopathy in T2DM patients with heart failure in India, resulting in a required sample size of approximately 92 patients.

Statistical method

Statistical analysis was performed using statistical package for the social sciences (SPSS) software version 20.0. Continuous variables such as age, BMI, HbA1c, and NT-proBNP were expressed as mean±standard deviation or median with interquartile range, depending on the distribution of the data. Categorical variables, including sex, diabetic retinopathy (DR) grades, heart failure (HF) subtypes, and NYHA functional class, were presented as frequencies and percentages. The Chi-square test was used to evaluate the association between categorical variables, particularly the relationship between the presence and severity of DR with the occurrence and types of HF. Analysis of variance (ANOVA) was employed to compare continuous variables across different grades of DR and HF subtypes. A p value of less than 0.05 was considered statistically significant.

RESULTS

The study included patients across a range of age groups, with the majority falling within the 50-69 years range. Specifically, 3 (3.26%) patients were below 40 years, 17 (18.47%) were aged 40-49 years, 34 (36.95%) were aged 50-59 years, 34 (36.95%) were aged 60-69 years, and 4 (4.34%) were aged 70 years and above. The mean age of the patients was 56.79 years (SD=8.32), with a range from 35 to 72 years (Table 1).

Table 2 presents the distribution of patients based on sex. Among the 92 patients, 49 (53.26%) were male, and 43 (46.73%) were female, showing a slightly higher proportion of male patients compared to female patients in the study.

Table 3 outlines the types of heart failure present in the patients. Among the 92 patients, 19 (20.65%) had no heart failure, 30 (32.6%) had heart failure with preserved ejection fraction (HFpEF), 23 (25%) had heart failure with mid-range ejection fraction (HFmrEF), and 20 (21.73%) had heart failure with reduced ejection fraction (HFrEF).

Table 1: Distribution of cases according to age of the patient (n=92).

Age of the patient (years)	Number of cases, N (%)
Below 40	3 (3.26)
40–49	17 (18.47)
50–59	34 (36.95)
60–69	34 (36.95)
70 and above	4 (4.34)
Mean age of the patient in years (SD)	56.79 (8.32)
Range	35–72

Table 2: Distribution of cases according to sex of the patient (n=92).

Sex of the patient	Number of cases (%)
Male	49 (53.26)
Female	43 (46.73)

Table 3: Distribution of cases according to type of heart failure (n=92).

Type of heart failure	Number of cases, N (%)
Absent	19 (20.65)
HFpEF	30 (32.6)
HFmrEF	23 (25)
HFrEF	20 (21.73)

Table 4 shows the distribution of patients based on the severity of diabetic retinopathy. Among the 92 patients, 18 (19.56%) had grade 0, indicating no retinopathy; 26 (28.26%) had grade 1, indicating mild non-proliferative diabetic retinopathy; 28 (30.43%) had grade 2, indicating moderate non-proliferative diabetic retinopathy; and 20 (21.73%) had grade 3, indicating severe non-proliferative diabetic retinopathy.

Table 5 shows the distribution of heart failure types (no heart failure, HFpEF, HFmrEF, HFrEF) across different grades of retinopathy. In grade 0 retinopathy, 9 (47.36%) patients had no heart failure, while 4 (13.33%) had HFpEF, 3 (13.04%) had HFmrEF, and 2 (10%) had HFrEF. For grade 1 retinopathy, 6 (31.57%) had no heart failure, 10 (33.33%) had HFpEF, 7 (30.43%) had HFmrEF, and 3 (15%) had HFrEF. In grade 2 retinopathy, 2 (10.52%) had no heart failure, 10 (33.33%) had HFpEF, 8 (34.78%) had HFmrEF, and 8 (40%) had HFrEF.

Lastly, in grade 3 retinopathy, 2 (10.52%) had no heart failure, 6 (20%) had HFpEF, 5 (21.73%) had HFmrEF, and 7 (35%) had HFrEF. The p value of 0.045 indicates a statistically significant association between the grade of retinopathy and the type of heart failure, with an increasing proportion of HFrEF as the grade of retinopathy worsen.

Table 4: Distribution of cases according to grade of diabetic retinopathy (n=92).

Diabetic retinopathy	Number of cases (%)
Grade 0	18 (19.56)
Grade 1	26 (28.26)
Grade 2	28 (30.43)
Grade 3	20 (21.73)

Table 6 presents the distribution of retinopathy in relation to the presence or absence of heart failure. Among patients with retinopathy, 64 cases (69.56%) had heart failure present, while 10 cases (10.86%) had heart failure absent, with a p value of 0.001, indicating a significant association between retinopathy and the presence of heart failure.

In contrast, among patients without retinopathy, 9 cases (9.78%) had heart failure present, and 9 cases (9.78%) had heart failure absent.

Table 5: Association of grade of retinopathy with type of heart failure (n=92).

Grade of retinopathy	No HF (%)	HFpEF (%)	HFmrEF (%)	HFrEF (%)	P value
Grade 0	9 (47.36)	4 (13.33)	3 (13.04)	2 (10)	0.045
Grade 1	6 (31.57)	10 (33.33)	7 (30.43)	3 (15)	
Grade 2	2 (10.52)	10 (33.33)	8 (34.78)	8 (40)	
Grade 3	2 (10.52)	6 (20)	5 (21.73)	7 (35)	

Table 6: Association of presence of retinopathy with heart failure (n=92).

Retinopathy	HF present (%)	HF absent (%)	P value
Present	64 (69.56)	10 (10.86)	0.001
Absent	9 (9.78)	9 (9.78)	

DISCUSSION

This study provides compelling evidence supporting a significant association between DR and HF in patients with T2DM. In our cohort, 80.43% of patients had DR, and 79.34% had HF, with a strong statistical association between the two (p=0.001). Moreover, we observed a progressive rise in the prevalence of HFrEF as DR severity increased (from 10% in grade 0 to 35% in grade 3), suggesting a dose-dependent relationship. These findings indicate that DR may not only reflect ocular microvascular disease but also serve as a surrogate marker of systemic vascular injury, including myocardial dysfunction.

Several previous studies have supported this association with Zhu et al, in a meta-analysis of over 100,000 patients,

demonstrated that DR significantly increases the risk of incident HF, particularly HFrEF, with a pooled relative risk of 2.10.[4] Similarly, Wong et al highlighted DR as a systemic marker of microvascular dysfunction, suggesting its utility in predicting macrovascular outcomes like HF and coronary artery disease.[2] Cheung et al, using data from the Atherosclerosis Risk in Communities (ARIC) study, found that DR independently predicted coronary heart disease and HF in patients without prior cardiovascular events.[1]

The pathophysiological link between DR and HF lies in their shared mechanisms. Chronic hyperglycemia leads to oxidative stress, endothelial dysfunction, and inflammation all of which damage the retinal and myocardial vasculature. Giacco and Brownlee emphasized the role of AGEs and reactive oxygen species in perpetuating vascular injury in diabetes.[3] These processes are also implicated in the development of myocardial fibrosis and left ventricular remodeling hallmarks of diabetic cardiomyopathy and HF.

Further supporting our findings, Brownrigg et al reported that microvascular complications, including DR, were independently associated with major adverse cardiovascular events, including HF, in a large UK-based T2DM cohort.[5] In a similar vein, Yau et al showed that DR prevalence was associated with higher cardiovascular mortality, reinforcing its role as a systemic disease marker.[6] A population-level cohort study by Wilkinson et al also established that DR severity correlates with higher incidence of cardiovascular events and mortality.[7]

Our data also showed that patients with more severe DR tended to have higher NYHA functional class, indicating reduced cardiac performance and physical tolerance. This supports the hypothesis presented by Paulus and Tschöpe, who proposed that systemic inflammation and microvascular endothelial dysfunction in comorbid conditions like T2DM contribute to HFpEF and later transition to HFrEF.[8] Importantly, most studies cited above were conducted in Western populations. Our study is among the few to explore this relationship in an Indian cohort, where the dual burden of diabetes and cardiovascular disease is growing rapidly. In contrast to previous studies, we also analyzed DR severity alongside HF subtypes, revealing a stepwise association—a finding with potential clinical implications.

The implications of our findings are significant. DR screening, typically reserved for ophthalmic management, could be integrated into cardiovascular risk assessment protocols. A simple fundoscopic exam may serve as an early, non-invasive tool for identifying diabetic patients at risk for heart failure, particularly in resource-limited settings. As highlighted by Ting et al, improving DR screening practices can enhance early diagnosis and intervention not only for vision-threatening disease but also for systemic vascular complications.[9]

Nonetheless, our study has limitations. The cross-sectional design limits causal inference, and the single-center nature may restrict generalizability. Also, although confounders were adjusted in analysis, residual confounding cannot be excluded. Future prospective studies are needed to evaluate whether treatment or regression of DR alters HF outcomes.

In conclusion, this study reinforces the growing body of evidence linking DR with HF, particularly HFrEF, in patients with T2DM. Our findings advocate for a multidisciplinary, integrated approach to diabetic care that recognizes DR as a systemic risk marker rather than an isolated ocular condition. Early identification of DR may prompt timely cardiovascular evaluation, risk modification, and potentially, prevention of adverse cardiac outcomes.

CONCLUSION

This study provides compelling evidence that DR serves as both a marker and potential mediator of HF risk in patients with T2DM. The robust association between DR severity and HF incidence, particularly HFrEF, highlights the systemic nature of diabetic vascular complications. Our findings demonstrate that retinal microvascular changes reflect parallel pathological processes occurring in the myocardium, likely driven by chronic hyperglycaemia, endothelial dysfunction, and low-grade inflammation.

The clinical implications are significant: routine ophthalmologic evaluation in diabetic patients offers a valuable opportunity for early cardiovascular risk stratification. These results call for a paradigm shift in diabetes management towards integrated care models that bridge ophthalmologic and cardiovascular monitoring. Future research should investigate whether targeted interventions for DR can modify HF progression, potentially opening new avenues for preventive cardiology in this high-risk population. Ultimately, these findings reinforce the importance of comprehensive, multi-disciplinary approaches to diabetes care that address both microvascular and macrovascular complications simultaneously.

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Cite this article as: Sharma P, Priyadarshi BP, Singh MP. Assessing the risk of heart failure in patients with diabetic retinupathy with type 2 diabetes mellitus. Int J Adv Med 2025;12:558-62.