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To study and analyze the association of diabetic retinopathy and its severity with left ventricular dysfunction and hypertrophy among type 2 diabetes mellitus patients – A hospital-based analytical cross-sectional study

Binayak Bibek Das[1]

[1]Department of Ophthalmology, Manipal Tata Medical College, Jamshedpur, Jharkhand, India.

***Corresponding author:**
Binayak Bibek Das
Senior Resident, Department of Ophthalmology, Manipal Tata Medical College, Jamshedpur, Jharkhand, India.

binayakbdas@gmail.com

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ABSTRACT

Objectives: Diabetes is among the prevalent contributors to vision loss. Due to similarity in their risk factors and pathophysiology, an association between diabetic retinopathy (DR) and cardiovascular events is expected. The objective of the study was to analyze the effects of different types of DR on left ventricular hypertrophy and dysfunction in patients with type 2 diabetes.

Material and Methods: A hospital-based analytical cross-sectional study was conducted from 2020 to 2022 in a tertiary care facility in Tamil Nadu, and it analyzed the data of patients with type 2 diabetes for over 5 years. The participants were divided into two groups: Non-proliferative DR (NPDR) and proliferative DR (PDR).

Results: In the present study, with respect to DR, the echo results showed a strong connection between the left ventricular mass, end diastolic diameter, mean E wave/A wave ratio, and mean isovolumetric relaxation time. There was also a correlation between the echo results and the volume of the mitral regurgitation jet. Furthermore, we found that 29 cases with left ventricular dysfunction (LVD) had NPDR, while 32 cases without LVD had PDR ($P < 0.05$).

Conclusion: Regular screening of all diabetic patients for potential complications, followed by strain echocardiography for high-risk individuals, is crucial for early detection and management. It is a cost-effective strategy for diagnosis, treatment, and prognosis. A key takeaway from this study is the importance of identifying high-risk patients during their asymptomatic stage by assessing microvascular complications.

Keywords: Diabetes mellitus, Left ventricular hypertrophy, Proliferative diabetic retinopathy, and non-proliferative diabetic retinopathy.

INTRODUCTION

Globally, diabetes mellitus (DM) has become one of the most significant public health challenges.[1] India is estimated to have more than 77.2 million prediabetics.[2] Projections indicate that by 2030, up to 79.4 million individuals in India may be affected by DM.[3] Consequently, the World Health Organization has labeled India as the global epicenter of diabetes. In addition, diabetes ranks among the primary causes of blindness in individuals aged 20–40.[4] Cataracts and retinopathy are widely recognized as common ocular complications associated with diabetes.

Chronic hyperglycemia causes the retinal vasculature to dysfunction. Diabetic retinopathy (DR), the resulting disease state, progresses gradually. It can be classified as either proliferative (PDR) or non-proliferative DR (NPDR). The 1st 5 years of type 1 diabetes are associated with a minimal risk of retinopathy. However, the prevalence increases significantly, with 27% of individuals who have had diabetes for 5–10 years and 71–90% of those with diabetes for over 10 years developing DR.

Coronary heart disease (CHD) stands as the leading cause of death among people with type 2 DM.[2] For these patients, the advancement of DR serves as an indicator of microvascular disease. The development of left ventricular hypertrophy (LVH) may play a role in increasing the occurrence of stroke, CHD, and heart failure. The chief determinants of LVH include obesity, increasing age, stature, chronic health disease, elevated blood pressure, cardiac valve diseases, and glucose intolerance.

LVH, as confirmed by an electrocardiogram and manifested by repolarization abnormality and elevated voltage, was a lethal finding; within a 5-year period, 33% of men and 21% of women were dead. ECG-LVH was linked to ventricular ectopy and a risk of sudden death comparable to that associated with CHD or cardiac failure. The increase in left ventricular mass acts as a crucial mechanism leading to adverse cardiovascular effects and heightened vulnerability to complications. The rise in left ventricular mass serves as a key pathway leading to negative effects on the cardiovascular system and increased susceptibility to complications. A growing body of evidence suggests that several heart diseases, including chronic heart diseases, ischemic heart diseases, heart failure, and sub-clinical indicators of cardiomyopathy, are associated with the presence of retinopathy, a condition easily and identified accurately through non-invasive photographic evaluation of the retina. Detecting retinopathy could also ameliorate personalized clinical risk evaluation for cardiovascular disease, over and beyond the known risk factors, in individuals with diabetes. Our research aimed to investigate the relationship between DR and its severity with left ventricular dysfunction (LVD) and hypertrophy in patients with type II DM. In addition, we sought to examine the factors associated with various grades of DR, LVD, and hypertrophy among individuals diagnosed with type 2 DM.

MATERIAL AND METHODS

This was an analytical cross-sectional study with a duration of 2 years in which all the patients who were over 40 years old with type 2 DM for more than 5 years visiting the hospital were enrolled in the study after obtained for written informed consent. We screened 100 patients and evenly divided them into two groups, each containing 50 patients: Group 1 (NPDR) and Group 2 (PDR).

The required diabetic history, treatment history, and relevant ocular history were obtained, and using Snellen's chart, the patients were examined thoroughly for visual acuity, anterior segment examined by the use of slit lamp, dilated fundus examination by slit lamp with 90 D lens, direct and indirect ophthalmoscope, fundus photograph was taken with a fundus camera, and optical coherence tomography (OCT) is done for the required patients. We graded the DR using the early treatment DR study system. The presence or absence of diabetic macular edema is also noted.

Echocardiogram: We used 2D Echocardiogram (ECHO) and doppler (DOPPLER) ultrasound (pulse wave and pulmonary vein) to determine ejection fraction, LV diastole dimension, LV systolic dimension, posterior wall thickness, LV mass, interventricular septal thickness, left atrial dimension, LV fractional shortening, pulse pressure/stroke volume index, mitral regurgitant jet volume calculation, peak A velocity, E wave/A wave (E/A) ratio calculation, peak E velocity, deceleration time, and isovolumetric relaxation time. We tabulated the ECHO and DOPPLER findings as well as DR staging for 100 patients, divided into two groups of 50 patients each, and studied the association between DR, LVD, and hypertrophy in type 2 DM patients.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences V.21. Depending on the type of distribution, we expressed continuous variables in terms of mean (standard deviation) or median (interquartile range). We expressed categorical variables as frequencies and percentages and plotted them. One-way analysis of variance was used to determine the association between the degrees of NPDR and LVD. We used the Chi-square test to determine the presence of any association between the three groups for categorical variables.

We present quantitative data using the mean with standard deviation, and we used an unpaired t-test to compare the study groups.

Using the Student's test and the Chi-square test, the association between the study groups was considered statistically significant if $P < 0.05$.

RESULTS

Ratio of male-to-female in NPDR cases was 2.1:1, while the ratio in PDR cases was 1.2:1. Males were more (62%) when compared to females (38%) [Tables 1-4]. The association was not significant.

According to age, most of the cases of NPDR were from the age group 51 to 60 years, while most cases of PDR were from the age group 40 to 50 years [Figure 1]. No significant association was inferred.

Table 1: Gender-wise distribution of study population.		
Gender	**Non-proliferative diabetic retinopathy**	**Proliferative diabetic retinopathy**
Male	34	28
Female	16	22
Total	50	50
Chi=1.528	*P*=0.216	NS

P value significance level is 0.05. NS: Non significant.

The patients in the present study were characterized into three groups: NPDR and PDR. According to the duration of diabetes, most of the cases had durations from 5 to 10 years (81%), while only 19% had durations more than 10 years [Figure 2].

According to severity, DR was categorized into mild, moderate, severe, and very severe NPDR, having 14, 17, 12, and 7 cases, respectively, and 50 cases were of PDR in our study [Figure 3].

In our study, a significant association was found in echo findings with respect to DR [Table 2]. Left ventricular mass in cases of NPDR and PDR was 145 g and 148 g, respectively.

A significant association was found between echo findings and mitral regurgitation jet volume, while no significant association was found with pulse pressure and stroke volume (SV)/pulmonary insufficiency (PI) [Table 3]. Pulse pressure of NPDR was 66 mm Hg, while that of PDR was 74 mm Hg. SV/pulse pressure (PP) of NPDR was 1.27, and that of PDR was value 1.21.

A significant association was found between LVD and DR. 29 cases with LVD had NPDR, while 32 cases without LVD had PDR [Table 4].

DISCUSSION

People with diabetes typically have a greater risk of heart-related issues compared to those without diabetes. It encompasses both systolic and diastolic heart failure, leading to more unfavorable results once symptomatic heart failure becomes evident.[2]

Our study's findings are consistent with prior research that categorized patients into three groups based on DR severity: Those without DR (NPDR; $n = 80$), those with simple retinopathy (severe DR [SDR]; $n = 20$), and those with PPDR or PDR ($n = 20$). Patients in the PPDR or PDR groups typically had a longer duration of diabetes and exhibited higher rates of neuropathy, elevated creatinine levels, increased urinary albumin clearance rate, and raised brain natriuretic peptide levels compared to individuals in the NPDR group. These outcomes align closely with those observed in similar studies.[2,3,5,6]

This study found significant associations between DR and the echo findings of left ventricular mass, left ventricular end diastolic

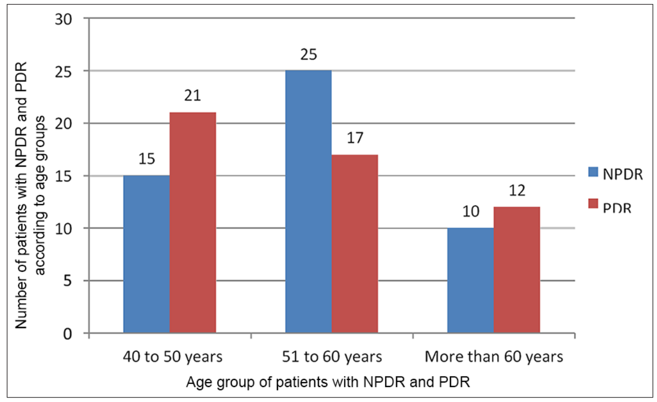

Figure 1: Distribution according to age group. NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy.

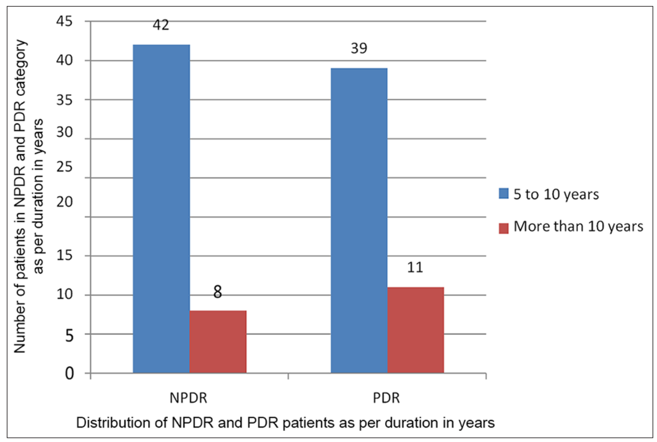

Figure 2: Distribution of patients according to duration of diabetes mellitus. NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy.

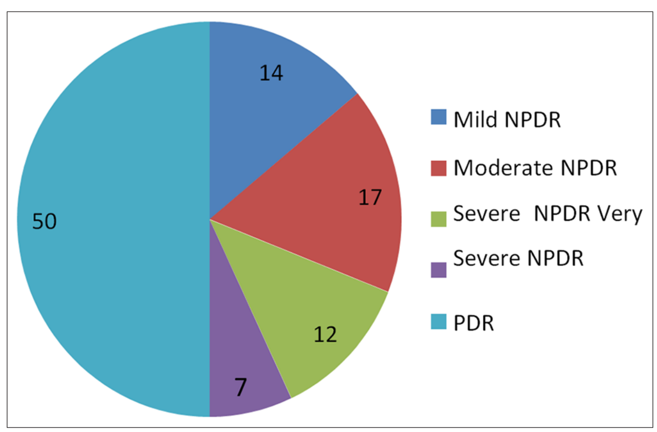

Figure 3: Distribution of patients according to types of diabetic retinopathy. NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy.

diameter, mean E wave/A wave ratio, and mean isovolumetric relaxation time. Unlike our study, the findings of Kennel WB

Table 2: Comparison of echocardiographic data with diabetic retinopathy.

Echo findings	Non-proliferative diabetic retinopathy	proliferative diabetic retinopathy	t-value	*P*-value
Left ventricular mass (g)	145 (32)	148 (41)	2.98	0.0036
Septal wall thickness (mm)	16.4 (4.2)	18.6 (3.1)	7.92	2.1
Posterior wall thickness (mm)	15.2 (1.9)	16.1 (2.1)	1.355	0.17
Left ventricular end-diastolic diameter (mm)	6.8 (1.4)	7.2 (1.5)	6.612	<0.0001
Mean peak E velocity (m/s)	0.8 (0.12)	0.89 (0.11)	3.9	0.0002
Mean peak A velocity (m/s)	0.38 (0.02)	0.28 9 (0.01)	28.77	<0.0001
Mean E/A ratio	2.4 (1.1)	1.9 (0.9)	2.488	0.0145
Mean deceleration time (m/s)	169 (40.1)	190 (46.5)	0.740	0.4612
Mean isovolumetric relaxation time (m/s)	79 (12.8)	81 (14.2)	2.418	0.0174

E/A: E wave/A wave ratio in echocardiography. *P* value significance level is 0.05

Table 3: Comparison of echocardiographic data with DR.

Echo findings	Non-proliferative diabetic retinopathy	Proliferative diabetic retinopathy	t-value	*P*-value
Pulse pressure mm Hg	66 (22)	74 (25)	1.699	0.092
Stroke volume/pulse pressure index (mL $beat^{-1}$ mm Hg^{-1})	1.27 (0.62)	1.21 (0.24)	0.638	0.524
Mitral regurgitation Jet Vmax (cm/s)	452 (88)	412 (92)	2.22	0.028
Mitral regurgitation Jet VTI (cm)	138.9 (21.7)	112.6 (19.6)	6.36	<0.0001

Vmax: Peak velocity of MR, VTI: Velocity time integral of MR, *P* value significance level is 0.05. MR: Mitral regurgitation, DR: Diabetic retinopathy

Table 4: Comparison of LVD with diabetic retinopathy.

LVD	Non-proliferative diabetic retinopathy	Proliferative diabetic retinopathy
LVD present	29	18
LVD absent	21	32
Chi=4.85	*P*=0.027	S

LVD: Left ventricular dysfunction

and Devereux RB revealed comparable results, with no patients exhibiting systolic impairment of left ventricular function (LVEF > 50%). Patients with severe DR (SDR) and PPDR or PDR had a significantly lower e0 (early diastolic mitral annular velocity) compared with those with NPDR (*P* =0.021).[7,8]

Consistent with our current investigation, recent epidemiological studies have revealed a direct link between DR and a heightened risk of heart failure, irrespective of factors such as diabetes duration, glycemic control, and both conventional and unconventional cardiovascular risk factors. However, the studies provided limited data on ventricular function. In our study of diabetic patients without heart failure, coronary artery disease, or cardiac symptoms, we found that e0 was lower in those with SDR, PPRD, or PDR than in those with NPDR. Furthermore, patients with PPDR or PDR had a larger E/e0 ratio than those with NPDR or SDR [Supplementary material].[9-12] People with mild to SDR have more noticeable left ventricular diastolic dysfunction (LVDD) than people without DR, according to three studies that evaluated the E/A ratio as a measure of left ventricular diastolic function in patients with diabetes who did not have coronary artery disease.[13-15]

According to a study that categorized patients according to their stage of DR (NPDR, SDR, PPDR, or PDR), people with DR had lower e0 than people without it. This implies that in people with DR, e0 can be a sign of the early alterations in left ventricular relaxation anomalies. The E/e0 ratio was much larger in the PPDR or PDR group than in the other two groups, although there was no discernible difference between patients with NPDR and SDR. According to this finding, patients with DR may have secondary changes in left ventricular relaxation anomalies that are reflected in the E/e0 ratio. These findings offer the first clinical proof that DR and LVDD are related.[16,17]

According to a study, patients with severe DR and DM had considerably reduced coronary flow reserve. This implies that DM patients with DR may have microvascular anomalies in their hearts, which could lead to diastolic dysfunction.[18]

CONCLUSION

This study found that in patients with type 2 DM, the presence of LVD and hypertrophy (LVH) was strongly correlated with the severity of DR. Based on the severity of DR, there were notable variations in echocardiographic measures such as left ventricular mass, diastolic dimensions, E/A ratio, isovolumetric relaxation time, and mitral regurgitation.

The presence of LVD was more likely in patients with NPDR, whereas those without LVD tended to have PDR.

These findings underscore the importance of routine screening for all diabetic complications, including DR. Strain echocardiography holds promise as a cost-effective tool for early diagnosis and risk stratification in high-risk patients. Most importantly, this study highlights the potential of identifying high-risk patients in their pre-symptomatic stages, based on the presence of microvascular complications like diabetic retinopathy (DR). It has to be dealt with pro-actively. Proactive management guided by these insights could significantly improve cardiovascular outcomes and prognosis in patients with diabetes.

Ethical approval: The research/study approved by the Institutional Review Board at Vinayaka Missions Kirupananda Variyar Medical College and Hospitals, number IEC/21/067, dated February 05, 2021.

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