Original Article

Evaluation of the Relationship Between Diabetic Retinopathy with the Severity of Coronary Artery Disease in Patients with Non ST Elevation Myocardial Infarction (NSTEMI)

Noor Din, Irshad Ahmed, Gohar Riaz, Aslam Latif Bhutto, Kheraj Matani and Naveedullah Khan

ABSTRACT

Objective: To determine the relationship between diabetic retinopathy with the severity of coronary artery disease in patients with non ST elevation myocardial infarction (NSTEMI)

Study Design: Randomized controlled Trial study

Place and Duration of Study: This study was conducted at the Department of National Institute of Cardiovascular Diseases (NICVD), Karachi, Sindh from August 2022 to January 2023.

Methods: In this observational cross-sectional study, 150 individuals diagnosed with NSTEMI and diabetes was enrolled. While in the hospital, these patients were examined with fundoscopic, which included fundal photography, and coronary angiograms.

Results: The gender distribution in the study population shows that 70.0% of the participants were male, while 30.0% were female. In Group I, the mean age was 56.5 ± 6.21. In Group II, the mean age was slightly lower at 54.8 ± 5.32 years. . Study found that smoking was (57.3% vs. 68%), hypertension (84.0% vs. 90.7%) were in the Diabetic & Retinopathy group and in the Non-diabetic & Retinopathy group respectively.

Conclusion: The results of the study reveal a substantial connection between diabetic retinopathy and angiographic severity of coronary artery disease (CAD) in NSTEMI patients.

Key Words: Coronary Angiography, Diabetic Retinopathy, Coronary Artery Disease, Prediction

INTRODUCTION

Cardiovascular diseases (CVDs) represent a critical global health challenge, and their prevalence in Pakistan, like many other countries, is a matter of significant concern. Epidemiological data highlights the alarming rise of CVDs in Pakistan over recent years.[1] This South Asian nation, with a population of over 220 million, is witnessing a notable surge in the incidence of heart diseases, primarily driven by factors such as sedentary lifestyles, unhealthy dietary habits, and an increasing aging population. CAD is a significant health concern in Pakistan, with a prevalence estimated to be around 10-15% of the adult population.[2,3]

Another well-known micro-angiopathic consequence of DM that is strongly linked to cardiovascular risk factors is diabetic retinopathy. Fundus images of the retina are the standard method of diagnosis. Microvascular pathology assessment utilizes a wide variety of qualitative markers. In the existence of diabetic health, the presence of diabetic retinopathy (DR) serves as a valuable indicator of broader vascular complications associated with diabetes, including coronary ischemia.[4,5] Significantly, individuals with type 2 diabetes who display signs of retinopathy are at an elevated risk of coronary heart disease (CHD), independently of factors like glycemic control, symptomatology, and other cardiovascular risk elements. Moreover, this heightened risk extends to an increased susceptibility to mortality and cardiovascular events.[6,7]

Patients diagnosed with Non-ST Elevation Myocardial Infarction (NSTEMI) present a unique clinical

Department of Interventional Cardiology, National Institute of Cardiovascular Diseases (NICVD), Karachi, Sindh.

Correspondence: Dr. Noor Din, Fellow of Interventional Cardiology, National Institute of Cardiovascular Diseases (NICVD), Karachi, Sindh.
Contact No: 03336663338
Email: galbistan@gmail.com

challenge in the presence of cardiovascular diseases.[8] However, it shares the same underlying cause – atherosclerotic plaque rupture or erosion – which leads to partial or intermittent coronary artery obstruction. The severity of coronary artery disease (CAD) can be measured using the Gensini score method, which was created by Gensini et al.[9]

The rationale for conducting this study lies in the quest for an efficient, non-invasive, and accurate method to predict the severity of coronary artery disease (CAD). Clinicians recognize the persistent need for a practical tool that can reliably assess the extent of coronary disease without resorting to invasive procedures.

METHODS

Following approval from the Institutional Review Board (NICVD/IRB/361) of the hospital where this research was conducted, specifically at the National Institute of Cardiovascular Diseases (NICVD) in Karachi, Sindh, the study took place from August 2022 to January 2023. The study included diabetic patients admitted to the hospital for non-ST-elevation myocardial infarction, who underwent fundoscopic examinations and fundal photography.

Each participant provided written informed consent. After having the pupils dilated with 1% tropicamide, a fundoscopic examination was performed. In addition, a fundal image was taken. Selected patients underwent coronary angiography, with the choice of intervention route determined by the operator. To ensure the accuracy and reliability of the Gensini scores, two independent and experienced interventional cardiologists were engaged in the assessment process. The statistical analysis was performed using SPSS, version 22.

RESULTS

Table No 1. The demographic composition in terms of age and gender among the study

Variables	Gender	NSTEMI & Diabetic Retinopathy	NSTEMI & Non-diabetic Retinopathy
Age	Mean±SD	56.5±6.21	54.8±5.32
	35-44	0 (0.0%)	4 (5.3%)
	45-54	28 (37.3%)	15 (20.0%)
	55-64	35 (46.7%)	49 (65.3%)
	65-74	12 (16.0%)	8 (10.7%)
Gender	Male 105(70.0%)	109(72.67%)	41(27.33%)
	Female 45(30.0%)	98(65.33%)	52(34.66)

The majority were male (70.0%), with a mean age of 56.5 years, while in the NSTEMI & Non-diabetic Retinopathy group, male representation was slightly

higher (72.67%), and the mean age was 54.8 years as shown in table 1.

Table No. 2: The distribution of study participants based on their risk factor profiles

Risk Factors	Diabetic & Retinopathy	Non-diabetic & Retinopathy	P-value
Smoking	43 (57.3%)	51 (68.0%)	0.42
Hypertension	63 (84.0%)	68 (90.7%)	0.19
Dyslipidemia	34 (45.3%)	28 (37.3%)	0.27
Family H/O of CAD	19 (25.3%)	9 (12.0%)	0.03*
Previous H/O of PAD	6 (8.0%)	6 (8.0%)	0.94
Previous H/O of CVD	6 (8.0%)	4 (5.3%)	0.56
Mean duration of DM (yrs.)	11.8±5.7	5.7±1.7	.001*
Patients taking insulin	44 (58.7%)	16 (21.3%)	0.003

Table No. 3: The categorization of study participants according to their Gensini score distribution

Gensini Score Categories	Diabetic retinopathy	Non-diabetic & retinopathy	p-value
Severe CAD (>36 points)	68 (90.7%)	35 (46.7%)	<0.001*
Not severe CAD (≤36)	7 (9.3%)	40 (53.3%)	<0.001*
Mean ± SD	63.3 ± 27.7	45.3 ± 25.3	

Table No. 4: The relationship between Diabetic Retinopathy and Gensini score, exploring how these two variables may be interconnected or influence each other.

No. of Vessels Involved	No. patients	Gensini Score (Mean ± SD)	p-value
No DR	75	43.35 ± 25.30	
Mild DR	16	48.69 ± 19.77	
Moderate DR	22	58.27 ± 23.87	<0.001
Severe Dr	22	75.98 ± 30.86	

The study revealed a notably longer mean duration of diabetes in the Diabetic & Retinopathy group (11.8±5.7 years) compared to the Non-diabetic & Retinopathy group (5.7±1.7 years), signifying a significant contrast shown in table 2. Furthermore, the mean Gensini Score was notably higher in the Diabetic Retinopathy group (63.3 ± 27.7) than in the Non-diabetic & Retinopathy group (45.3 ± 25.3), indicating a significant difference

in CAD severity between the two groups as shown in table 3. As the severity of Diabetic Retinopathy increases, there is a noticeable upward trend in the mean Gensini Score. Specifically, individuals with "No DR" have the lowest mean Gensini Score (43.35 ± 25.30), followed by those with "Mild DR" (48.69 ± 19.77), "Moderate DR" (58.27 ± 23.87), and "Severe DR" (75.98 ± 30.86). Univariate analysis showed, a longer duration of Diabetes mellitus was associated with a slightly increased odds of the outcome (OR = 1.14) with a p-value of 0.02*. Smoking, hypertension (HTN), and dyslipidemia did not exhibit significant associations in the univariate analysis given in table 5.

Table No. 5: Univariate and multivariate logistic regression to determine factors influencing Gensini score-based coronary artery disease severity

Variables	OR(95% CI) Univariate Analysis	P-value	OR(95% CI) Multivariate Analysis	p-value
Duration of Diabetes mellitus	1.14(1.025 – 1.279)	0.02*	0.88(0.725 –1.075)	0.31
• Insulin taking	1.17(1.05 –2.976)	0.03*	0.62(0.164 – 2.331)	0.46
• Serum creatinine	4.46 (1.435 – 28.620)	0.02*	2.29(0.219 – 24.14)	0.82
Diabetic Retinopathy (+)	8.41(3.148 – 22.517)	0.001*	13.03(2.410 – 70.419	0.001*
Smoking	0.725(0.414 – 1.271)	0.289	—	—
HTN	1.006(0.567 - 1.784)	0.277	—	—
Dyslipidemia	0.887(0.478 – 1.645)	0.711	—	—

DISCUSSION

For individuals with type-2 diabetes, cardiovascular disease is the leading cause of death, resulting in a mortality rate roughly three times higher than that observed in the general population. The presence of diabetic retinopathy in diabetes patients was identified as a predictor for the onset of coronary artery disease events and was associated with an increased risk of coronary artery disease.[10, 11]

In our study, the majority of participants were male (70.0%), with a mean age of 56.5 years. In the NSTEMI and Non-diabetic Retinopathy group, the male representation was slightly higher at 72.67%, and the mean age was 54.8 years. The distribution of age and gender in both groups closely mirrored the findings of a study conducted by Norgaz et al. (2015).[12] These results are consistent with the study by Pathak et al. (2021) conducted in Nepal.

Our study found that smoking was (57.3% vs. 68%), hypertension (84.0% vs. 90.7%), hypertension (84.0% vs. 90.7%) rates were in the Diabetic & Retinopathy group and in the Non-diabetic & Retinopathy group respectively with insignificant difference. our study revealed a notably longer mean duration of diabetes in the Diabetic & Retinopathy group (11.8±5.7 years) compared to the Non-diabetic & Retinopathy group (5.7±1.7 years), signifying a significant contrast. This closely resembles the research conducted by Saleem et al. (2008).[14] & Fox et al, (2014).[15] Our findings were also in line with Agrawal et al. (2016) there wasn't a notable correlation observed between Diabetes Mellitus (DM), hypertension, smoking, lipid levels, or obesity in distinguishing between STEMI and NSTEMI groups.[16]

In our study, the mean Gensini Score demonstrated a notable increase in the Diabetic Retinopathy group (63.3±27.7) compared to the Non-diabetic Retinopathy group (45.3±25.3), indicating a significant disparity in the severity of coronary artery disease (CAD) between the two groups. This observation aligns with similar trends reported in other studies; for instance, Al Amin et al. (2022) found a mean Gensini score of 62.2±27.7 for Group I and 43.3±25.3 for Group II, reaffirming a consistent pattern.[17] Furthermore, a separate investigation by Rong J et al. (2012), revealed a substantial increase in the prevalence of coronary atherosclerosis among individuals with T2DM who also had diabetic retinopathy.[18]

In our research paper, univariate analysis, longer Diabetes duration (OR = 1.14, 95% CI: 1.025 - 1.279), insulin use (OR = 1.17, 95% CI: 1.05 - 2.976), and elevated serum creatinine (OR = 4.46, 95% CI: 1.435 - 28.620) were associated with the outcome, while Diabetic Retinopathy showed a strong association (OR = 8.41, 95% CI: 3.148 - 22.517). These results were comparable with Al Amin et al. (2022).[17] & Cheung et al. (2007) had previously reported analogous findings.[19] To validate the severity of CAD outcomes, future research should consider conducting similar studies in larger population centers with a broader range of variables.

CONCLUSION

The results of the study reveal a substantial connection between diabetic retinopathy and angiographic severity of coronary artery disease (CAD) in NSTEMI patients. This relationship suggests that diabetic retinopathy could be viewed as an independent predictor of the severity of coronary artery disease.

Author's Contribution:

Concept & Design of Study:	Noor Din
Drafting:	Irshad Ahmed, Gohar Riaz
Data Analysis:	Aslam Latif Bhutto,

	Kheraj Matani, Naveedullah Khan
Revisiting Critically:	Noor Din, Irshad Ahmed
Final Approval of version:	Noor Din

REFERENCES

1. Brant LCC, Nascimento BR, Veloso GA, Gomes CS, Polanczyk C, Oliveira GMMD, et al. Burden of Cardiovascular diseases attributable to risk factors in Brazil: data from the" Global Burden of Disease 2019" study. Revista da Sociedade Brasileira de Medicina Tropical 2022;55:e0263-2021.
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol 2020;76(25):2982-3021.
3. Ruan Y, Guo Y, Zheng Y, Huang Z, Sun S, Kowal P, et al. Cardiovascular disease (CVD) and associated risk factors among older adults in six low-and middle-income countries: results from SAGE Wave 1. BMC Public Health 2018;18(1):1-3.
4. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Molecular Sciences 2020;21(17):6275.
5. Batista TM, Haider N, Kahn CR. Defining the underlying defect in insulin action in type 2 diabetes. Diabetologia 2021;64:994-1006.
6. Xie J, Ikram MK, Cotch MF, Klein B, Varma R, Shaw JE, et al. Association of diabetic macular edema and proliferative diabetic retinopathy with cardiovascular disease: a systematic review and meta-analysis. JAMA Ophthalmol 2017;135(6):586-93.
7. Hsu CY, Lee CM, Chou KY, Lee CY, Chen HC, Chiou JY, et al. The association of diabetic retinopathy and cardiovascular disease: a 13-year nationwide population-based cohort study. Int J Environmental Res Public Health 2021;18(15):8106.
8. Sia CH, Zheng H, Ho AF, Bulluck H, Chong J, Foo D, et al. The Lipid Paradox is present in ST-elevation but not in non-ST-elevation myocardial infarction patients: Insights from the Singapore Myocardial Infarction Registry. Scientific Reports 2020;10(1):6799.
9. Sinning C, Lillpopp L, Appelbaum S, et al. Angiographic score assessment improves cardiovascular risk prediction: the clinical value of SYNTAX and Gensini application. Clin Res Cardiol 2013;102(7):495-503.
10. Kengne AP, Patel A, Colagiuri S, Heller S, Hamet P, Marre M, et al. The Framingham and UK Prospective Diabetes Study (UKPDS) risk equations do not reliably estimate the probability of cardiovascular events in a large ethnically diverse sample of patients with diabetes: the Action in Diabetes and Vascular Disease: Preterax and Diamicron-MR Controlled Evaluation (ADVANCE) Study. Diabetologia 2010;53:821-31.
11. Vetrone LM, Zaccardi F, Webb DR, Seidu S, Gholap NN, Pitocco D, et al. Cardiovascular and mortality events in type 2 diabetes cardiovascular outcomes trials: a systematic review with trend analysis. Acta diabetologica 2019;56:331-9.
12. Norgaz T, Hobikoglu G, Aksu H, et al. Retinopathy is related to the angiographically detected severity and extent of coronary artery disease in patients with type 2 diabetes mellitus. Int Heart J 2015;46(4):639-646.
13. Pathak SR, Gajurel RM, Poudel CM, Shrestha H, Thapa S, Koirala P. Angiographic Severity of Coronary Artery Disease in Diabetic and Non-Diabetic Acute STEMI Patients in a Tertiary Care Centre of Nepal. Kathmandu Univ Med J 2021;19(4):410-4.
14. Saleem T, Mohammad KH, Abdel-F MM. Association of glycosylated haemoglobin level and diabetes mellitus duration with the severity of coronary artery disease. Diab Vasc Dis Res 2008;5(3):184-9.
15. Fox CS, Sullivan L, D'Agostino RB, Wilson PW. The significant effect of diabetes duration on coronary heart disease mortality: the Framingham Heart study. Diabetes Care 2014;27(3):704-8.
16. Agrawal V, Lohiya BV, Sihag BK, Prajapati R. Clinical profile with angiographic correlation in naïve acute coronary syndrome. J Clin Diagnostic Res : JCDR. 2016;10(9):OC10.
17. Al Amin H, Choudhury AK, Ahsan SA, Dutta B, Hossain MM, Alam N, et al. Association of Diabetic Retinopathy with Angiographic Severity of Coronary Artery Disease in Patients with Non-ST Elevation Myocardial Infarction. Univ Heart J 2022;18(1):50-3.
18. Rong J, Yu C, Yang P, Chen J. Association of retinopathy with coronary atherosclerosis determined by coronary 64-slice multi-detector computed tomography angiography in type 2 diabetes. Diabetes Vascular Disease Res 2012;10(2):161-168.
19. Cheung N, Wang JJ, Klein R, Couper DJ, Sharrett AR, Wong TY. Diabetic retinopathy and the risk of coronary heart disease: the Atherosclerosis Risk in Communities Study. Diabetes Care 2007;30:1742-1746.