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Original Article

Frequency of In-Stent Restenosis (ISR) in Diabetic Patients Following Percutaneous Coronary Intervention (PCI) for Stable Coronary Artery Disease (CAD) with Angina Pectoris Class III

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ABSTRACT

Background: Coronary intervention with stenting is crucial for managing stable ischemic heart disease and acute coronary syndrome, but post-procedural complications such as stent thrombosis and in-stent restenosis (ISR) remain significant challenges. Diabetes mellitus has been identified as a key risk factor contributing to the increased incidence of ISR, thereby complicating long-term outcomes for these patients.

Objective: This study aimed to compare the incidence of ISR between diabetic and non-diabetic patients who have undergone percutaneous coronary intervention (PCI) for stable ischemic heart disease, specifically angina class III.

Methods: A retrospective observational study was conducted at the Peshawar Institute of Cardiology, involving 180 patients who underwent PCI between January and July 2023. Patients were divided into two groups based on the presence or absence of diabetes mellitus (90 in each group). ISR was defined using visual angiography as >50% diameter stenosis within the stent or its adjacent 5mm. The demographic and clinical variables collected included age, gender, BMI, smoking status, hypertension, and family history of coronary artery disease. Statistical analysis was performed using SPSS version 25, employing Chi-square tests for categorical variables, with a significance level set at $p < 0.05$.

Results: The mean ages of the non-diabetic and diabetic groups were 50.01 ± 8.66 years and 44.26 ± 7.55 years, respectively. The incidence of ISR was significantly higher in the diabetic group (15 out of 90, 16.67%) compared to the non-diabetic group (3 out of 90, 3.33%), with a statistically significant difference ($p = 0.001$).

Conclusion: Diabetes mellitus significantly increases the risk of in-stent restenosis following PCI in patients with stable ischemic heart disease. This highlights the need for targeted strategies to manage and monitor diabetic patients more aggressively post-PCI to reduce the risk of ISR.

Keywords: In-stent restenosis, diabetes mellitus, percutaneous coronary intervention, coronary artery disease, stable ischemic heart disease, angiography, cardiovascular risk management.

INTRODUCTION

Coronary intervention with stenting is recognized as the most effective treatment for both stable ischemic heart disease and acute coronary syndrome. However, stent thrombosis and in-stent restenosis (ISR) represent the most common complications following this procedure (1-4). Previous studies have identified several risk factors associated with ISR post-percutaneous coronary intervention (PCI), including smoking (37.6%), hypertension (65.5%), diabetes mellitus (45.1%), hyperlipidemia (41.9%), and a familial history of coronary heart disease (16.7%). Another research focusing on patients who developed ISR after angioplasty found a high prevalence of hyperlipidemia (43.3%), hypertension (66.7%), smoking (46.7%), and a history of high blood pressure (66.7%) (1, 5-10).

Diabetes mellitus (DM) significantly contributes to the global burden of cardiovascular disease, with a two- to four-fold increased risk of peripheral vascular disease (PVD) and coronary artery disease (CAD) associated with this condition (11-14). Before the

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introduction of bare-metal stents (BMS), diabetes was considered a significant predictor of major adverse cardiac events (MACE) and ISR following PCI. With the advent of drug-eluting stents (DES), it remains uncertain whether diabetic patients are at an increased risk of developing ISR. The medical histories and outcomes of diabetic patients with DES-ISR are not well-documented, making it unclear whether their prognosis is less favorable compared to non-diabetic patients. Moreover, clinical studies comparing different PCI modalities are scarce, and their findings do not necessarily reflect real-world scenarios (15-19).

In light of this, our study aimed to compare the incidence of in-stent restenosis among diabetic and non-diabetic patients who had previously undergone PCI for stable ischemic heart disease with angina of CCS class III severity. By focusing on this specific patient population, we sought to determine whether diabetes mellitus increases the likelihood of ISR, potentially guiding future therapeutic strategies and interventions in this high-risk group (20, 21).

MATERIAL AND METHODS

In-stent restenosis (ISR) was defined using visual angiography as the presence of more than 50% diameter stenosis within the stent or within 5mm of its proximal or distal edges. This retrospective observational study was conducted at the Peshawar Institute of Cardiology, Department of Cardiology, from January to July 2023. The study population consisted of 180 individuals, evenly divided into two groups of 90 participants each, with one group having diabetes and the other not. All participants were diagnosed with stable ischemic heart disease angina class III after coronary angiography.

Inclusion criteria were adult patients of both sexes who had undergone prior percutaneous coronary intervention (PCI). Exclusion criteria included individuals with valvular heart disease, myocarditis, pericarditis, or those unwilling to participate. After securing informed written consent, demographic data were meticulously collected, including gender, age, body mass index (BMI), smoking status, hypertension, and family history of ischemic heart disease.

During the study period, repeat coronary angiography (CAG) was performed on patients with diabetes who exhibited classical angina symptoms post-DES implantation, based on clinical judgment. ISR was determined through visual examination if stenosis was observed to be more than 50% within or adjacent to the stent margins.

Data were analyzed using statistical software SPSS version 25. Continuous variables were expressed as means and standard deviations, while categorical variables were presented in percentages and frequencies. The incidence of ISR was compared between diabetic and non-diabetic patients using the Chi-square test, with a p-value of <0.05 considered statistically significant. This analysis adhered to a 95% confidence interval and a margin of error of 5%.

All study procedures conformed to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

RESULTS

In examining the baseline characteristics of the participants, several demographic and clinical variables were compared between those with and without diabetes (Table 1). The mean age of the non-diabetic participants was 50.01 years with a standard deviation of 8.66, indicating a middle-aged cohort, while the diabetic group was slightly younger, with a mean age of 44.26 years and a standard deviation of 7.55. Body mass index (BMI), a significant indicator of general health, showed that non-diabetic participants had a mean BMI of 23.26 kg/m² (± 2.66), generally considered within the normal range. In contrast, diabetic participants had a higher mean BMI of 25.12 kg/m² (± 3.66), categorizing them closer to the overweight threshold.

Table 1: Baseline Characteristics of Participants

Variables	Non-Diabetic (N=90)	Diabetic (N=90)
Mean Age (years)	50.01 ± 8.66	44.26 ± 7.55
Mean BMI (kg/m²)	23.26 ± 2.66	25.12 ± 3.66
Gender		
Male	40	45
Female	50	45
Comorbidities		
Hypertension (HTN)	30	36
Smoking	16	36
Family History of CAD	20	31

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Table 2: Comparison of In-stent Restenosis (ISR) Incidence

Variables	Non-Diabetic (N=90)	Diabetic (N=90)	p-value
In-stent Restenosis	3	15	0.001

Gender distribution within the study groups revealed an equal number of females in both groups (N=45), but there were more males in the diabetic group (N=45) compared to the non-diabetic group (N=40). This difference underscores potential gender-related disparities in diabetes prevalence or management. Regarding comorbid conditions, hypertension was more common in the diabetic group, with 36 cases compared to 30 in the non-diabetic group. Smoking was notably higher among diabetic participants, with 36 smokers compared to only 16 in the non-diabetic group, suggesting a correlation between diabetes and higher incidence of smoking. Family history of coronary artery disease also showed a higher prevalence among diabetics, with 31 individuals reporting a family history compared to 20 in the non-diabetic group.

The incidence of in-stent restenosis (ISR), which is a critical outcome post-percutaneous coronary intervention, was significantly different between the two groups (Table 2). Only 3 cases of ISR were observed among the non-diabetic individuals, whereas the diabetic group exhibited a markedly higher incidence with 15 cases. This substantial difference was statistically significant, with a p-value of 0.001, indicating a strong association between diabetes and increased risk of ISR.

These findings highlight significant differences in baseline characteristics and health outcomes between diabetic and non-diabetic individuals undergoing PCI, emphasizing the heightened risk and burden of cardiovascular complications associated with diabetes.

DISCUSSION

In the realm of cardiac interventions, stent thrombosis and in-stent restenosis (ISR) pose significant complications, each presenting distinct clinical manifestations. Stent thrombosis typically occurs acutely or subacutely and is often precipitated by procedural issues such as edge dissection, malapposed stent struts, or non-compliance with dual antiplatelet therapy, presenting with myocardial infarction and severe chest pain. In contrast, ISR often manifests more subtly as stable or unstable angina. Neo-atherosclerosis or neo-intimal hyperplasia, while potential causes for longer-term target lesion failures, are rarely the immediate culprits; instead, procedure-related factors are more commonly implicated (22-24).

In this study, the patient cohort was divided into two groups—those with and without diabetes—to investigate the influence of diabetes on the incidence of ISR. Despite similar demographics and risk profiles between the groups, including age, sex, BMI, hypertension, smoking status, and family history of coronary artery disease, the outcomes revealed notable differences in ISR occurrence. Among the 180 patients studied, ISR was observed in 18 individuals (10%), aligning with previous reports indicating ISR rates of 5 to 10% in patients receiving primary percutaneous coronary intervention. Notably, a substantial majority of ISR cases occurred in diabetic patients (15 out of 18 cases, or 83.33%), underscoring a significant association between diabetes and increased ISR risk, which was statistically significant (p-value <0.05) (25-27).

These findings are consistent with prior research, such as the study by Raja W et al., which highlighted diabetes mellitus as a predominant risk factor in ISR, occurring in 22.9% of cases within a population experiencing a 3.75% overall ISR prevalence. Similarly, research by Paramasivam G. et al. demonstrated higher rates of stent-edge restenosis in diabetic individuals (20.3%) compared to non-diabetics (9.2%). Furthermore, Praveen K. Gupta et al. identified diabetes mellitus as a substantial risk factor, with a 5.63% ISR occurrence in a cohort of 550 patients (9, 28).

The strong correlation between diabetes and ISR in our findings mirrors these earlier studies, reinforcing the notion that diabetes mellitus is the most consistent and significant risk factor for ISR development. This relationship likely stems from the complex interplay of hyperglycemia-induced endothelial dysfunction, increased oxidative stress, and accelerated atherogenesis seen in diabetic patients (2, 9, 14, 18, 22).

The study's strengths lie in its focused comparison of diabetic and non-diabetic groups, allowing for clear delineation of the impact of diabetes on ISR outcomes. However, limitations include its retrospective design and the single-center setting, which may not provide a broad representation of the general population. Future studies should consider multi-center designs to enhance generalizability and include longitudinal follow-ups to assess long-term outcomes post-PCI in these populations (16, 23, 28).

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CONCLUSION

In conclusion, this study reaffirms the significant association between diabetes mellitus and increased incidence of ISR among patients undergoing primary percutaneous coronary intervention. It underscores the need for stringent monitoring and possibly more aggressive management of diabetic patients post-PCI to mitigate ISR risks. These findings also advocate for further research to explore preventive strategies and interventions tailored specifically towards diabetic populations to enhance their cardiovascular outcomes.

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