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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

IBRAHIM SHAH[1], UMAR IBRAHIM PARACHA[2], SAIF ULLAH[3], SAMIULLAH KHAN[4], MATIULLAH KHAN[5], AKHTAR SHER[6]
[1]*Associate Professor of Cardiology, Gajju Khan Medical College / Bacha Khan Medical Complex, Swabi*
[2]*Assistant Professor of Cardiology Gajju Khan Medical College /Bacha Khan Medical Complex, Swabi*
[3]*Consultant Cardiologist, Department of Cardiology, Pak Medical Center and Hospital, Peshawar*
[4]*Associate Professor, Department of Cardiology, DHQ Teaching Hospital/Bannu Medical College, Bannu*
[5]*Assistant Professor/Consultant Cardiologist, Department of Cardiology, DHQ Teaching Hospital, Swabi*
[6]*Assistant Professor, Department of Cardiology, Gajju Khan Medical College / DHQ Teaching Hospital, Swabi*
Correspondence to: Ibrahim Shah, Email: ibrahimshahcpsp@gmail.com

ABSTRACT

Background: In-stent restenosis (ISR) remains a significant concern following percutaneous coronary intervention (PCI), particularly among diabetic patients who are at higher risk due to underlying vascular and metabolic factors. This research sought to establish the prevalence of ISR among diabetic patients with stable coronary artery disease and assess the relevant clinical and operative variables.

Methods: A cross-sectional analytical study was conducted at Gajju Khan Medical College/Bacha Khan Medical Complex Swabi and Pak Welfare Cardiac Cath Lab, Peshawar, from February 2022 to January 2023. A total of 110 diabetic patients who underwent PCI for stable CAD and returned for follow-up coronary angiography were included. Clinical profiles, angiographic characteristics, and stent details were reviewed. ISR was defined as ≥50% narrowing within or near the stented segment. Statistical analysis was performed to identify associations between ISR and various risk factors.

Results: ISR was detected in 25.4% of patients. Factors significantly associated with ISR included poor glycemic control (HbA1c ≥7%), longer duration of diabetes, dyslipidemia, triple vessel disease, long lesions, small vessel diameter, and use of longer or smaller stents. Symptom recurrence and the need for repeat revascularization were remarkably more prevalent among patients diagnosed with ISR.

Conclusion: Diabetic patients remain at high risk for ISR despite the use of modern stent technologies. Recognizing clinical and angiographic predictors can help guide preventive strategies and improve patient outcomes following PCI.

Keywords: 'In-stent restenosis, diabetes mellitus, percutaneous coronary intervention, coronary artery disease, drug-eluting stents, angioplasty, risk factors'

INTRODUCTION

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide, with a particularly high burden in low- and middle-income countries. Among various treatment strategies, PCI with stent placement has become a cornerstone in the management of patients with stable angina[1, 2]. However, despite technological advancements, one of the major challenges following PCI is the development of ISR, which can lead to recurrent symptoms and the need for further revascularization[3].

Diabetes mellitus is a well-established risk factor for both the development and progression of CAD. It is also strongly associated with a higher risk of adverse outcomes after PCI, including restenosis[4]. The pro-inflammatory and pro-thrombotic state in diabetes, along with endothelial dysfunction and accelerated atherosclerosis, contributes to neointimal hyperplasia, which is the primary mechanism behind ISR[5]. Although drug-eluting stents have significantly reduced ISR rates compared to bare-metal stents, diabetic patients continue to experience restenosis at a higher frequency than non-diabetics[6].

Identifying patients at risk for ISR is essential to improving clinical outcomes[7]. Factors such as lesion length, vessel diameter, stent size, and glycemic control may all play a role in determining the likelihood of restenosis. In settings where access to advanced imaging and individualized procedural planning may be limited, understanding these associations becomes even more critical[8].

This study aims at assessing the prevalence of in-stent restenosis among diabetics with stable CAD undergoing PCI, while also assessing the clinical, angiographic, and procedural correlates of this condition. The ultimate goal was to improve the risk assessment and management strategies in diabetic patients with CAD when intervened through coronary arteries.

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METHODOLOGY

This is a cross-sectional analytical study held in two centers: Gajju Khan Medical College/Bacha Khan Medical Complex Swabi and Pak Welfare Cardiac Catheterization Laboratory, which is attached to Pak Medical Center and Hospital Peshawar. The time frame of the study was one year starting from February 2022 to January 2023. The study was approved by the ethical review boards of both centers. Patient confidentiality was ensured, and all material was used exclusively for the research. Consent was gathered where necessary.

The main goal was to assess the rate of ISR among patients suffering from diabetes and who had PCI performed on them due to stable CAD with accompanying angina pectoris. Patients were selected using non-probability consecutive sampling. A total of 110 diabetic patients who had previously undergone PCI and later presented for follow-up coronary angiography were included in the study.

Patients were eligible if they had a documented diagnosis of type 1 or type 2 diabetes mellitus and had undergone PCI with stent placement for stable CAD. Only those who returned for follow-up coronary angiography within 6 to 12 months after the initial procedure were included, allowing for the detection of ISR. Both genders and patients aged 30 to 75 years were considered.

Patients were excluded if they had undergone PCI for acute coronary syndromes (e.g., STEMI or NSTEMI), had non-diabetic status, or lacked complete angiographic records. Those with stent thrombosis, graft interventions, or those lost to follow-up were also excluded.

Patient demographics, clinical history, and procedural details were obtained from hospital records and catheterization lab databases. Variables such as age, gender, duration of diabetes, HbA1c levels, history of hypertension, smoking status, and lipid profiles were recorded. Angiographic features including the number of diseased vessels, target artery, lesion length and type, vessel diameter, and stent details (type, length, diameter) were reviewed from angiographic images interpreted by two

independent cardiologists.In-stent restenosis was defined as ≥50% diameter stenosis within the stented segment or up to 5 mm beyond its margins, as confirmed by follow-up coronary angiography. Time to ISR development and need for repeat revascularization were also documented.

Data were analyzed using statistical software. Continuous variables were expressed as means with standard deviations, while categorical variables were presented as frequencies and percentages. The association between ISR and different clinical, angiographic, and procedural factors was tested using 'chi-square or Fisher's exact test for categorical variables and independent t-test or Mann-Whitney U test' for continuous variables, depending on normality. A p-value of less than 0.05 was considered statistically significant.

RESULT

The demographic data reveal that the mean age of patients who developed in-stent restenosis (ISR) was significantly higher compared to those who did not (59.3 ± 8.1 vs. 56.1 ± 7.9 years, p = 0.041). Although a greater proportion of males were present in both groups, the gender distribution did not differ significantly. Obesity, defined as BMI ≥ 30, was more frequent among ISR patients, though not statistically significant. The distribution of residence (urban vs. rural) also showed no meaningful difference. These findings suggest that increasing age may be an independent factor associated with ISR in diabetic individuals, while gender and residence appear unrelated.

Table 1: Demographic Characteristics of Patients (n = 110)

Variable	ISR Present (n = 28)	ISR Absent (n = 82)	p-value
'Age (years), Mean ± SD'	59.3 ± 8.1	56.1 ± 7.9	0.041*
Gender (Male)	21 (75%)	58 (70.7%)	0.678
BMI ≥ 30 (Obese)	12 (42.9%)	22 (26.8%)	0.102
Urban Residence	18 (64.3%)	45 (54.9%)	0.385

*Statistically significant at p < 0.05

In terms of clinical characteristics, patients with a longer duration of diabetes (≥10 years) were significantly more likely to develop ISR (60.7% vs. 35.4%, p = 0.017). Similarly, poor glycemic control, indicated by HbA1c levels ≥7%, was strongly associated with ISR (82.1% vs. 50.0%, p = 0.003). The presence of dyslipidemia was also more prevalent among the ISR group (67.9% vs. 43.9%, p = 0.031). While hypertension, smoking history, and family history of CAD were common, these did not show significant associations. These observations suggest that long-standing and poorly controlled diabetes, along with lipid abnormalities, may play key roles in promoting restenosis post-PCI

Table 2: Clinical Characteristics of Patients

Variable	ISR Present (n = 28)	ISR Absent (n = 82)	p-value
Duration of Diabetes ≥ 10 yrs	17 (60.7%)	29 (35.4%)	0.017*
HbA1c ≥ 7%	23 (82.1%)	41 (50.0%)	0.003*
Hypertension	22 (78.6%)	55 (67.1%)	0.260
Dyslipidemia	19 (67.9%)	36 (43.9%)	0.031*
Smoking (Current/Former)	11 (39.3%)	24 (29.3%)	0.317
Family History of CAD	15 (53.6%)	33 (40.2%)	0.206

Angiographic characteristics showed that triple vessel disease was significantly more frequent among patients who developed ISR (32.1% vs. 15.9%, p = 0.048), implying that diffuse atherosclerosis might contribute to restenosis. Lesions longer than 20 mm and small vessel diameter (<2.5 mm) were also significantly associated with ISR (p = 0.004 and p = 0.008 respectively), highlighting the role of lesion complexity and vessel size in stent failure. Although complex lesion types (Type C) more prevalent in the ISR group, the difference did not achieve statistical significance. These angiographic observations overall support the view that anatomical features and lesion shape are major determinants of the risk of ISR.

Table 3: Angiographic and Lesion Characteristics

Variable	ISR Present (n = 28)	ISR Absent (n = 82)	p-value
Triple Vessel Disease	9 (32.1%)	13 (15.9%)	0.048*
LAD as Target Vessel	20 (71.4%)	52 (63.4%)	0.456
Lesion Length ≥ 20 mm	18 (64.3%)	27 (32.9%)	0.004*
Small Vessel Diameter (<2.5mm)	15 (53.6%)	21 (25.6%)	0.008*
Complex Lesion (Type C)	13 (46.4%)	22 (26.8%)	0.065

Procedure-related variables revealed that patients receiving longer stents (≥28 mm) and stents with smaller diameters (<3 mm) were significantly more likely to develop ISR (p = 0.015 and p = 0.017, respectively). Although drug-eluting stents were predominantly used in both groups, their use was slightly lower in the ISR group, approaching statistical significance (p = 0.060). Post-dilation did not significantly affect ISR occurrence. These data indicate that mechanical and device-related factors, such as stent length and diameter, may influence restenosis risk, even in the presence of modern drug-eluting stents.

Table 4: Interventional Procedure Details

Variable	ISR Present (n = 28)	ISR Absent (n = 82)	p-value
Drug-Eluting Stent Used	21 (75%)	73 (89%)	0.060
Stent Length ≥ 28 mm	14 (50.0%)	20 (24.4%)	0.015*
Stent Diameter < 3 mm	13 (46.4%)	18 (22.0%)	0.017*
Post-Dilation Done	9 (32.1%)	34 (41.5%)	0.375

Table 5: ISR and Clinical Outcomes

Outcome	ISR Present (n = 28)	ISR Absent (n = 82)	p-value
Symptom Recurrence (Angina)	20 (71.4%)	9 (11.0%)	<0.001*
Time to ISR (months), Mean ± SD	7.2 ± 2.5	—	—
Repeat Revascularization Needed	16 (57.1%)	0	<0.001*

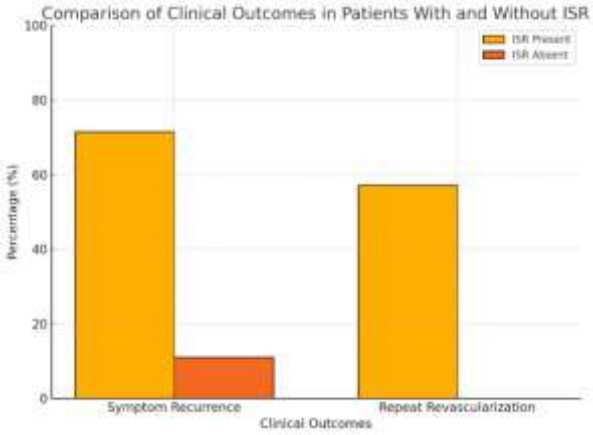

Figure 1**:** Assessment of clinical outcomes of patients with diabetes and without diabetes with in-stent restenosis. The illustration displays increased incidences of repeat angina and revascularization procedures in those who had ISR after the PCI procedure.

Clinical outcomes showed a stark contrast between the two groups. Among patients who developed ISR, 71.4% experienced symptom recurrence in the form of angina, compared to only 11.0% in the 'non-ISR group (p < 0.001)'. Moreover, 57.1% of ISR patients required repeat revascularization, whereas none of the patients without ISR needed this intervention (p < 0.001). The average time to ISR detection was 7.2 ± 2.5 months. These outcomes emphasize the clinical burden of ISR, translating into

recurrent symptoms and a higher likelihood of undergoing additional invasive procedures.

DISCUSSION

This study aimed to evaluate the frequency of in-stent restenosis (ISR) in diabetic patients undergoing percutaneous coronary intervention (PCI) for stable coronary artery disease (CAD) and to explore the contributing factors. The findings revealed a notable ISR rate in this high-risk population, with several clinical and angiographic features showing significant associations.

One of the key observations was the relationship between poor glycemic control and ISR. A significantly higher proportion of patients who developed ISR had HbA1c levels above 7%, reflecting suboptimal long-term blood sugar management. This supports previous literature indicating that hyperglycemia accelerates neointimal hyperplasia and endothelial dysfunction, both of which contribute to restenosis. Studies have similarly highlighted poor glycemic control as a predictor of ISR, particularly in the era of drug-eluting stents[9-11].

Longer duration of diabetes was also found to be significantly associated with ISR, aligning with prior research suggesting that chronic metabolic stress leads to more diffuse atherosclerosis and exaggerated vascular response to injury[12-14]. Additionally, dyslipidemia was more prevalent among ISR patients, emphasizing the role of lipid abnormalities in promoting vascular inflammation and plaque progression post-PCI.

Angiographic characteristics also played an important role. ISR was more frequently seen in patients with longer lesions, small-caliber vessels, and multi-vessel disease. These findings are in line with previous studies which reported higher restenosis rates in complex coronary anatomies[15-17]. Longer stents and smaller diameters were also linked with increased ISR, likely due to impaired drug delivery and higher risk of stent underexpansion.

Interestingly, even while drug-eluting stents were employed with the majority of patients, ISR took place, particularly in patients with longer stents or smaller vessels. This implies that although relatively modern equipped stents have lead to lower ISR rates, they still do not mitigate the risk entirely, particularly amongst the more difficult diabetic patients with several comorbidities and complex lesions. The ISR group had a fairly significant rate of symptom recurrence as well as needing repeat revascularization, which is really important clinically[18-20].

This analysis agrees with existing literature but also sheds new light on the local population[21]. Metabolic control and careful stent selection along with individualized procedural planning amongst diabetic patients is of utmost importance which is further demonstrated by the high ISR rates. This could be due to lack of proper follow-up and secondary prevention measures and restricted imaging techniques during PCI.

This study offer useful insights but still contains certain boundaries. The cross-sectional study did not determine causality. In addition, due to a lack of resources, intravascular imaging devices like IVUS or OCT, which would have enhanced lesion evaluation and stent refinement, were not used regularly. With longer follow-up periods and the inclusion of imaging-guided PCI, other studies could better examine ISR patterns in diabetics.

CONCLUSION

This study focuses the significant burden of in-stent restenosis for patients suffering with diabetes, for whom PCI is performed for stable coronary artery disease. Poor glycemic control, greater duration of diabetes, dyslipidemia, complex lesion morphology, and the use of longer or narrower stents were found to be the major contributory factors. Despite advancements in stent technology, diabetic patients are still at a high risk for restenosis and repeat surgical interventions. These results highlight the need for enhanced metabolic control, thorough lesion evaluation, and specific interventional approaches to mitigate ISR and improve long term results in this high risk diabetes patients.

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