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Major Adverse Cardiovascular Events in Insulin- Versus Non-Insulin-Treated Type 2 Diabetes Patients Following Percutaneous Coronary Intervention: A Prospective Cohort Study

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ABSTRACT

Background: Insulin-treated type 2 diabetes millatus (ITDM) is associated with heigher cardiovascular risk profile. However its impact on major adverse cardiovascular events (MACE) following poorer percutaneous coronary intervention (PCI) remains unclear.

Aims: This study aimed to evaluate major adverse cardiovascular events in insulin-treated diabetes mellitus (ITDM) and non-insulin-treated diabetes mellitus (Non-ITDM) type 2 diabetes mellitus (T2DM) patients' post-PCI.

Methods: A single-center prospective cohort study was conducted in which 465 T2DM patients undergoing PCI and completing the 1-year follow-up were enrolled. Patients were divided into two groups based on their therapy for DM: ITDM and Non-ITDM. The primary endpoint was MACE, a composite of non-fatal myocardial infarction (MI), stroke, coronary artery bypass grafting (CABG), repeat PCI, and mortality.

Results: Logistic regression confirmed higher odds of MACE among ITDM compared to Non-ITDM patients (unadjusted OR = 1.743, 95% CI: 0.865–3.512, $p = 0.120$; adjusted OR = 1.729, 95% CI: 0.822–3.635, $p = 0.149$). Kaplan–Meier analysis illustrated increased cumulative incidence of MACE among ITDM over 12 months (Log rank $p = 0.113$). Similarly, Cox proportional hazards analysis reported higher hazard ratios in the insulin-treated group (unadjusted HR = 1.695, 95% CI: 0.874–3.284, $p = 0.118$; adjusted HR = 1.554, 95% CI: 0.793–3.045, $p = 0.199$). Yet the results were not statistically significant. Overall, a higher incidence of MACE was reported among ITDM (12.5%) compared to Non-ITDM (7.5%), particularly repeat PCI (4.8% vs. 2.5%) and stroke (3.8% vs. 1.4%) among T2DM patients after PCI.

Conclusion: T2DM patients receiving insulin therapy had a higher incidence of adverse cardiovascular events compared to those not on insulin treatment, that insulin-treated patients may represent a higher-risk group for MACE following PCI.

1 | Introduction

Diabetes is a metabolic disorder characterized by elevated blood glucose, mainly due to insulin resistance and relative insulin deficiency due to pancreatic dysfunction, presenting as two types requiring different treatments. According to WHO, the treatment of diabetes can be classified into insulin-treated diabetes mellitus (ITDM) and Non-insulin-treated diabetes mellitus (Non-ITDM) [1, 2]. ITDM is defined as the condition in which blood glucose level is maintained by the use of external insulin [1], as autoimmune dysfunction of the pancreas does not produce enough insulin required for survival. Insulin therapy is prescribed in DM when oral anti-diabetic medications fail to control glucose or when complications develop, such as diabetic ketoacidosis, neuropathy, or retinopathy [3, 4]. It is also crucial for type 2 diabetes mellitus (T2DM) patients with β-cell dysfunction and inadequate insulin secretion [5, 6].

However, the use of insulin decreases the microvascular complications in patients [7], but it increases weight gain and dyslipidemia, which are directly linked to cardiovascular disease (CVD) risk, ultimately leading to a higher incidence of major advesre cardiovascular events (MACE) in diabetic patients [8, 9]. The ACCORD trial reported that diabetic patients who were maintaining their strict glycemic level with high doses of insulin had more chances of cardiovascular (CV) death due to low blood glucose levels and higher stress [10]. Similarly, more MACE with hypoglycemia and more weight gain were noticed among insulin glargine users in ORIGIN trial [11]. This is because most diabetic patients begin using insulin in the latter stages of diabetes mellitus (DM), where comorbid conditions, including chronic kidney disease and anemia, are highly prevalent [3, 12].

Also, among diabetics, the usage of insulin is directly associated with poorer cardiovascular outcomes after percutaneous coronary intervention (PCI) compared to patients taking oral hypoglycemic medications [13, 14]. According to published research, individuals using insulin had a greater risk of negative outcomes following PCI than those receiving oral hypoglycemic medications [15–17]. A review reported direct costs of CV complications increased 20% to 49% in diabetic patients [18]. In Mexico, 439,523 million pesos cost is estimated due to DM and CVD complications, while this cost can be reduced up to 174,085 million with early [19].

However, recent studies show that after adjusting for propensity scores, the cardiovascular risk in insulin-treated diabetic patients is reduced [20]. The increased cardiovascular risk is more linked to underlying health conditions rather than insulin therapy itself [21]. In contrast, another study reported that, after propensity score matching, ITDM patients had a higher risk of developing CVDs compared to Non-ITDM patients [22]. Many factors explained this elevated risk: insulin therapy is associated with atherosclerosis due to insulin resistance, endothelial dysfunction, oxidative stress, and inflammation [15, 22, 23]. Elevated glucose levels enhance platelet aggregation and reduce fibrinolytic activity, increasing the likelihood of thrombotic events like Myocardial infraction (MI) [24]. Additionally, vascular smooth muscle proliferation accelerates restenosis post-PCI [25]. Moreover, recent data suggest a higher frequency of target lesion revascularization (TLR) in patients receiving newly developed drug-eluting stents (DES) [26].

Although insulin is crucial for blood glucose management, its effects on cardiovascular outcomes in patients with T2DM and ischemic heart disease remain a subject of ongoing investigation. Previous large meta-analyses have evaluated the association between insulin therapy and cardiovascular outcomes, providing robust evidence at a global level [27]. However, data from South Asian populations undergoing PCI are limited, and prospective studies with systematic follow-up are scarce. Consequently, the current study aimed to assess the incidence of MACE in ITDM and Non-ITDM patients undergoing PCI, [13].

2 | Materials and Methods

2.1 | Study Design, Setting, and Duration

A prospective cohort study design was adopted, this design tracks a cohort over time to gather information on exposures and monitor outcomes. The present study was performed at the Punjab Institute of Cardiology, Lahore, a tertiary healthcare institute in Punjab province of Pakistan. data were collected from patients admitted to hospital wards for PCI from September 20, 2023, to January 20, 2024, and follow-up was made for the next 12 months of each patient from the date of enrollment.

Participants were included in the study of any gender and aged ≥ 18 years, with acute MI (STEMI/NSTEMI and unstable angina) and post-procedural Thrombolysis in MI- grade 3 flow, with T2DM. Participants were excluded with a prior history of MI, CABG, or PCI, with hemoglobinopathies, hemolytic anemia, HIV, chronic kidney disease, pericardial disease, valvular heart disease, cardiogenic shock, ST-elevation ECG without clear signs of CAD such as acute myocarditis, early repolarization, or Takotsubo cardiomyopathy, and with T1DM.

2.2 | Study Sample

A standard cohort study formula using Epi-Info was used to determine the required sample size. The researchers reported that a sample size of 480 was appropriate, based on the prevalence of MACE in T2DM patients undergoing PCI, with a 95% confidence interval (CI) and 80% power. Participants who completed the study follow-up were included in the final analysis. Consecutive sampling technique was adopted to choose sample units, in which all eligible participants were enrolled during the study period until the required sample size was achieved.

2.3 | Study Instrument

The data collection tool was developed through a multi-phase process to ensure validity and appropriateness for assessing clinical and demographic characteristics of T2DM patients undergoing PCI with DES, and also evaluate MACE during follow-up.

2.3.1 | *Literature Review and Conceptual Framework*

A thorough literature review of previous studies was conducted, and followed clinical guidelines to identify patients' socio-demographic factors, previous medical records, factors that accelerate CAD, glycemic control (Hemoglobin Aic (HbA1c)) monitoring, and cardiovascular outcomes. This guided the main structure and scope of the questionnaire to ensure that it has all the required domains to fulfill the study criteria.

2.3.2 | *Initial Drafting*

A structured data collection form was developed with the consultation of a cardiology expert and with the guidance of academic supervisors. It comprised eight sections:

- Socio-demographic data (age, gender, BMI, education, income, etc.)
- Medical history (including therapy of DM, diabetes duration, hypertension, dyslipidemia, smoking status, and family history)
- Risk factors for coronary heart disease (smoking, hypertension, dyslipidemia, etc.)
- Laboratory investigations (HB, RBG, HbA1c, etc.)
- Disease-related information (angiographic findings, stent details)
- Pharmacotherapy after PCI
- Outcomes during follow-up (non-fatal MI, repeat PCI, CABG, stroke, and cardiac death).

2.3.3 | *Translation and Expert Validation*

The structured data collection form included data extracted from patient profiles, which required no translation, as well as patient-reported outcomes, which were administered in Urdu and back-translated to ensure linguistic and cultural accuracy. Face and content validity were assessed by a panel of five experts (two cardiologists, one epidemiologist, and two senior faculty members) who reviewed the form for clarity, relevance, and comprehensibility. Minor revisions were made to improve wording, formatting, medical terminology, and the logical flow of questions, ensuring the tool was clear and appropriate for participants with varying literacy levels.

2.3.4 | *Pilot Testing*

To evaluate the flow, clarity, and feasibility of the prepared data collection form in a real clinical setting, a pilot test was performed with 35 eligible participants, who were not included in main sample of 480. Their feedback was noted regarding difficulty in understanding or clarity of the questions, and all the important modifications were made in the final study tool.

2.3.5 | *Final Refinement and Approval*

A final version of the data collection tool was approved by the supervisory committee after incorporating all relevant suggestions from experts and participants, and it was used for data collection.

2.4 | Data Collection Procedure

A systematic and standardized process was adopted to maintain the integrity, consistency, and reliability of data collection.

2.4.1 | *Collection of Baseline Information*

At baseline, essential information of each participant, including demographic, clinical, and laboratory data were collected using the structured data collection form to provide a foundation for outcome assessment.

2.4.2 | *Patient Stratification and Grouping*

Data were collected from participants with type T2DM undergoing intracoronary stent placement using conventional percutaneous methods. According to treatment records and clinical history, patients receiving insulin therapy, either alone or in combination with oral hypoglycemic agents, were classified as having ITDM, while those managed exclusively with oral hypoglycemic medications were classified as Non-ITDM. For patients with an established diabetes history, current treatment modality and duration of insulin use were confirmed during data collection precedure. Participants were then divided into two groups based on their insulin treatment status: ITDM and Non-ITDM.

2.4.3 | *Questionnaire Administration*

Key patient information, including demographics, medical history, risk factors, and so forth, was extracted from patient profiles and recorded on a structured data collection form. Clinical outcomes were obtained directly from patients using the same form. Standardized instructions ensured consistency, and for patients unable to attend in person during follow-up, outcomes were collected via telephone to maximize completeness.

2.4.4 | *Ensuring Data Accuracy*

Collected data were systematically entered and verified to ensure accuracy. Data entry and verification procedures, including cross-checking by independent researchers, ensured data integrity. Research team members involved in verification were trained in data validation and handling incomplete responses.

2.4.5 | *Primary Outcomes of the Study*

Clinical outcomes, including non-fatal MI, stroke, CABG, repeat PCI, and cardiac death, were systematically recorded after 6 months and again after 12 months post-procedure to ensure uniform follow-up.

2.4.6 | *Handling of Missing Data*

During follow-up, 15 patients were lost, including 13 non-respondents and 2 who died of non-cardiac causes. These patients were excluded from the final outcome analysis to maintain data integrity.

2.5 | Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 21.0, Armonk, NY:

IBM Corp.). A significance threshold of $p < 0.05$ was applied to determine statistical significance in all tests. To ensure the reliability and accuracy of results, the data were double-checked for outliers and errors. Descriptive statistics were used to summarize data. Continuous variables were expressed as mean ± SD and categorical variables were presented as absolute frequencies and percentages. Inferential statistics based on the normality of the data was applied for analysis to evaluate the incidence of MACE among patients stratified by therapy of DM. Comparisons were performed across groups of therapy of DM, along with demographic and baseline clinical characteristics of responding participants using Chi-square tests for categorical variables and Kruskal–Wallis test for continuous variables. Furthermore, binary Logistic regression analysis was performed, both as univariate (unadjusted) and multivariate (adjusted) analysis, to explore the odds of MACE to evaluate the association of ITDM and Non-ITDM patients with MACE. Survival analysis was performed using unadjusted Kaplan–Maier analysis (outcomes reported as log-rank test) and Cox-proportional hazard analysis, both as univariate (unadjusted) and multivariate (adjusted) analysis, expressed as adjusted hazard ratios (HRs) with 95% CI to estimate time-to-event data and understand the particular risk of an event (MACE) during a 12-month follow-up.

3 | Results

3.1 | Sociodemographic and Baseline Clinical Characteristics of Patients Stratified by ITDM and Non-ITDM

The socio-demographic and baseline clinical characteristics of all 465 participants included in this study are presented in Table 1A–1D, and were stratified by therapy of DM (insulin-treated and non-insulin-treated). No significant differences were observed in gender, age, BMI, or education between the two groups. However, monthly income differed significantly ($p = 0.007$), with a higher proportion of insulin-treated patients earning more than 60,000 (Table 1A).

Clinical parameters like EF and hemoglobin were not significantly different ($p > 0.05$), but insulin-treated patients had significantly higher random blood glucose and HbA1c levels ($p = 0.000$), indicating poor glycemic control. Moreover, the duration of diabetes (> 10 years) was significantly longer among insulin-treated patients ($p = 0.048$). No significant difference was found in ECG findings (NSTEMI, STEMI, unstable angina), number of diseased vessels, number of stents passed, or type of procedure ($p > 0.05$) (Table 1B).

Medical history and risk factors like smoking, hypertension, and dyslipidemia also had no significant association with therapy of DM, except cerebrovascular disease, which was significantly higher in insulin-treated patients (10.4% vs. 4.5%, $p = 0.022$) (Table 1C).

Medication usage showed significant differences. Use of oral hypoglycemic drugs ($p = 0.000$), lipid-lowering agents ($p = 0.028$), and anti-anginal drugs ($p = 0.040$) varied across groups. Most insulin-treated patients were on metformin alone and atorvastatin, while Non-ITDM patients were more often prescribed combination therapies and rosuvastatin. Nitrates + ranolazine were also more commonly used in Non-ITDM patients (Table 1D).

3.2 | Incidence of MACE in ITDM Versus Non-ITDM Patients Following PCI

Table 2 presents the incidence of MACE among 465 participants with T2DM following PCI, comparing ITDM and Non-ITDM patients. The prevalence of non-fatal MI was 1.0% in ITDM and 1.4% in Non-ITDM. CABG was only performed in Non-ITDM

TABLE 1A | Sociodemographic characteristics of patients stratified by therapy of DM.

Demographic characteristics		ITDM ($N = 106$)	Non-ITDM ($N = 359$)	Total ($N = 465$)	p value
Gender	Male	77 (72.6)	253 (70.5)	330 (71.0)	0.666
	Female	29 (27.4)	106 (29.5)	135 (29.0)	
Age	18–24	0 (0.0)	5 (1.4)	5 (1.1)	0.576
	25–44	10 (9.6)	41 (11.4)	51 (11.0)	
	45–60	67 (63.2)	213 (59.3)	280 (60.2)	
	> 60	29 (27.4)	100 (27.9)	129 (27.7)	
Body mass index	< 18.5	11 (10.6)	43 (12.0)	54 (11.6)	0.560
	18.5–24.9	44 (41.5)	168 (46.8)	212 (45.6)	
	25–29.9	36 (34.0)	97 (27.0)	133 (28.6)	
	30–39.9	15 (14.2)	51 (14.2)	66 (14.2)	
Education	≤ Primary	45 (42.5)	145 (40.4)	190 (40.9)	0.284
	Secondary	35 (33.0)	148 (41.2)	183 (39.4)	
	Graduate	26 (24.5)	66 (18.4)	92 (19.8)	
Monthly income	≤ 60,000 (low/medium)	65 (61.3)	274 (76.3)	339 (72.9)	0.007
	> 60,000 (high)	41 (38.7)	85 (23.7)	126 (27.1)	

Abbreviation: BMI, body mass index.

TABLE 1B | Baseline clinical characteristics of patients stratified by duration of DM.

Baseline clinical characteristics					
Ejection fraction		51 ± 10.170	51.62 ± 9.837	51.48 ± 9.928	0.666
Hemoglobin		13.41 ± 1.285	13.30 ± 1.287	13.31 ± 1.282	0.437
Random blood glucose level		301.29 ± 80.300	271.13 ± 78.950	278 ± 80.860.	0.000
HbA1c at the time of PCI	≤ 6.5	4 (3.8)	48 (13.4)	52 (11.2)	0.000
	6.6−7	11 (10.4)	79 (22.0)	90 (19.4)	
	7.1−7.5	21 (19.8)	91 (25.3)	112 (24.1)	
	7.6−8	36 (34.0)	89 (24.8)	125 (26.9)	
	> 8	34 (32.1)	52 (14.5)	86 (18.5)	
ECG	Unstable angina	11 (10.4)	37 (10.3)	48 (10.3)	0.837
	NSTEMI	61 (57.7)	216 (60.2)	277 (59.6)	
	STEMI	34 (32.1)	106 (29.5)	140 (30.1)	
Duration of DM (years)	< 5	38 (35.8)	125 (34.8)	163 (35.1)	0.048
	5−10	22 (20.8)	114 (31.8)	136 (29.2)	
	> 10	46 (43.4)	120 (33.4)	166 (35.7)	
vessels showing CAD	Single-vessel	30 (28.3)	118 (32.8)	148 (31.8)	0.541
	Multi-vessel (DVD + TVD)	76 (71.7)	241 (67.2)	317 (68.2)	
Number of stent pass	One	28 (26.4)	121 (33.7)	149 (32.0)	0.361
	≥ 2 (two or more)	78 (73.6)	238 (66.3)	316 (68.0)	
Type of procedure	Emergency	19 (17.9)	64 (17.8)	83 (17.8)	0.982
	Elective	87 (82.1)	259 (82.2)	382 (82.2)	

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; DVD, double vessel disease; ECG, electrocardiogram; ITDM, insulin-treated diabetes mellitus; Non-ITDM, non-insulin-treated diabetes mellitus; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; TVD, triple vessel disease.

TABLE 1C | Baseline medical history and risk factors of patients stratified by duration of DM.

Medical history					
Cardiovascular diseases	Yes	56 (52.8)	184 (51.3)	240 (51.6)	0.775
Heart failure	Yes	28 (26.4)	93 (25.9)	121 (26.0)	0.916
Cerebrovascular disease	Yes	11 (10.4)	16 (4.5)	27 (5.8)	0.022
COPD	Yes	9 (8.5)	31 (8.6)	40 (8.6)	0.963
Peripheral artery disease	Yes	17 (16.0)	35 (9.7)	52 (11.2)	0.079
Diabetic ulcer	Yes	7 (6.6)	19 (5.3)	26 (5.6)	0.606
Diabetic neuropathy	Yes	26 (24.5)	74 (20.6)	100 (21.5)	0.389
Covid-19	Yes	10 (9.4)	58 (16.2)	68 (14.6)	0.085
Covid-19 vaccination	Yes	49 (46.2)	136 (37.9)	185 (39.8)	0.123
Risk factors					
Smoker	Yes	41 (38.7)	131 (36.5)	172 (37.0)	0.682
hypertension	Yes	60 (56.6)	191 (53.2)	251 (54.0)	0.537
Dyslipidaemia	Yes	21 (19.8)	77 (21.4)	98 (21.1)	0.717
Family history of CAD	Yes	31 (29.2)	91 (25.3)	122 (26.2)	0.423
Alcohol intake	Yes	6 (5.7)	16 (4.5)	22 (4.7)	0.816

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CVD, cardiovascular diseases.

(1.4%). Repeat PCI was more frequent in ITDM (4.8%) versus Non-ITDM (2.5%). Stroke (3.8% vs. 1.4%) and death (2.9% vs. 0.8%) were also more common in insulin users. Overall, the total MACE rate was higher in ITDM (12.5%) compared to Non-ITDM (7.5%). These results were graphically presented in Figure 1.

3.3 | Association of MACE With Therapy of DM Following PCI

Binary logistic regression (univariate and multivariate) was applied to assess the association of MACE with insulin treatment. The Hosmer–Lemeshow test showed good model fit

TABLE 1D | Baseline medications of patients stratified by duration of DM.

Medications					
Oral hypoglycemic drugs	Biguanides (Metformin only)	66 (62.3)	30 (8.4)	96 (20.6)	0.000
	SGLT-2 inhibitors (alone)	0 (0.0)	10 (2.8)	10 (2.2)	
	Sulfonylureas & DPP-4 inhibitors	3 (2.8)	14 (3.9)	17 (3.7)	
	Combination therapy	9 (8.5)	303 (84.4)	312 (67.1)	
Lipid-lowering drugs	Atorvastatin	28 (26.4)	68 (18.9)	96 (20.6)	0.028
	Rosuvastatin	75 (70.8)	289 (80.5)	364 (78.3)	
Rate-limiting drugs	Beta blockers	98 (92.5)	311 (86.6)	409 (88.0)	0.091
	None or other	8 (7.5)	48 (13.4)	56 (12.0)	
Anti-hypertensive drugs	CCB & CCB + ACI	42 (39.6)	121 (33.7)	163 (35.1)	0.565
	ACI, ARB & other	21 (19.8)	70 (19.5)	91 (19.6)	
Anti-anginal drugs	Nitrates only	36 (34.9)	125 (34.8)	162 (34.8)	0.040
	Nitrates + Ranolazine or Trimetazidine	14 (13.2)	81 (22.6)	95 (20.4)	
Diuretics	Furosemide	17 (16.0)	53 (14.8)	70 (15.1)	0.944
	Furosemide + Aldactone	17 (16.0)	60 (16.7)	77 (16.6)	
	None	72 (68.3)	246 (68.2)	318 (68.4)	
Anti-platelets	Disprin + Clopidogrel	102 (96.2)	354 (98.6)	456 (98.1)	0.118
	Disprin + Ticagrelor	4 (3.8)	5 (1.4)	9 (1.9)	

Abbreviations: ACI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DPP-4, dipeptidyl peptidase-4; SGLT-2, sodium–glucose cotransporter-2.

TABLE 2 | Incidence of MACE in ITDM versus Non-ITDM patients following PCI.

	Treatment of diabetes mellitus	
Major adverse cardiovascular events	**ITDM ($N = 106$)**	**Non-ITDM ($N = 359$)**
Non-fatal MI	1 (1.0)	5 (1.4)
CABG	0 (0.0)	5 (1.4)
Repeat PCI	5 (4.8)	9 (2.5)
Stroke	4 (3.8)	5 (1.4)
Death	3 (2.9)	3 (0.8)
Total MACE	13 (12.5)	27 (7.5)

Abbreviations: CABG, coronary artery bypass grafting; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

($p = 0.243$), and the Nagelkerke R^2 of 0.143 indicated that the adjusted model explained 14.3% of the variance in MACE. In univariate analysis, ITDM patients had higher odds of MACE (OR = 1.743, 95% CI: 0.865–3.512; $p = 0.120$). After adjustment for age, gender, BMI, smoking, hypertension, dyslipidemia, history of CVDs, HbA1c, LVEF, duration of diabetes, and medications, a similar trend persisted (adjusted OR = 1.729, 95% CI: 0.822–3.635; $p = 0.149$), though not statistically significant, indicating a potentially higher risk in the ITDM group (Table 3).

Survival analysis was performed to estimate time-to-event data and understand the particular risk of an event (MACE) during a 12-month follow-up, using the Kaplan—Meier survival curve and Cox proportional hazard analysis. The Kaplan–Meier plot showed a higher cumulative incidence of MACE in ITDM patients, with divergence becoming more apparent after 4 months, although the log-rank test was not significant ($p = 0.113$). Cox regression supported these findings: univariate HR = 1.695 (95% CI: 0.874–3.284; $p = 0.118$) and adjusted HR = 1.554 (95% CI: 0.793–3.045; $p = 0.199$). While not statistically significant, both models indicated a trend toward higher MACE risk among insulin-treated patients after PCI (Figure 2, Table 3).

4 | Discussion

The present study examined the relationship between the types of T2DM treatment, ITDM versus Non-ITDM, and the incidence of MACE after PCI. Given the rising prevalence of T2DM and coronary artery disease globally, understanding the impact of treatment type on cardiovascular outcomes is essential. This study provides insight into how sociodemographic factors, baseline clinical characteristics, comorbidities, medication use, and 12-month survival relate to treatment choice. While some associations did not reach statistical significance, they highlight clinically relevant trends. Our findings suggest that insulin-treated patients may be at greater risk of adverse cardiovascular outcomes, potentially due to longer disease duration, poorer glycemic control, and higher comorbidity burden.

Baseline sociodemographic and clinical characteristics have a strong association with DM therapy and MACE risk. In our results, there were no significant differences in the type of treatment as per age or gender, consistent with studies reporting a similar incidence of cardiovascular events whether patients are treated with or without insulin, irrespective of gender or age [28–30]. Although a meta-analysis of over 5 million patients showed that diabetes increases the risk of coronary heart

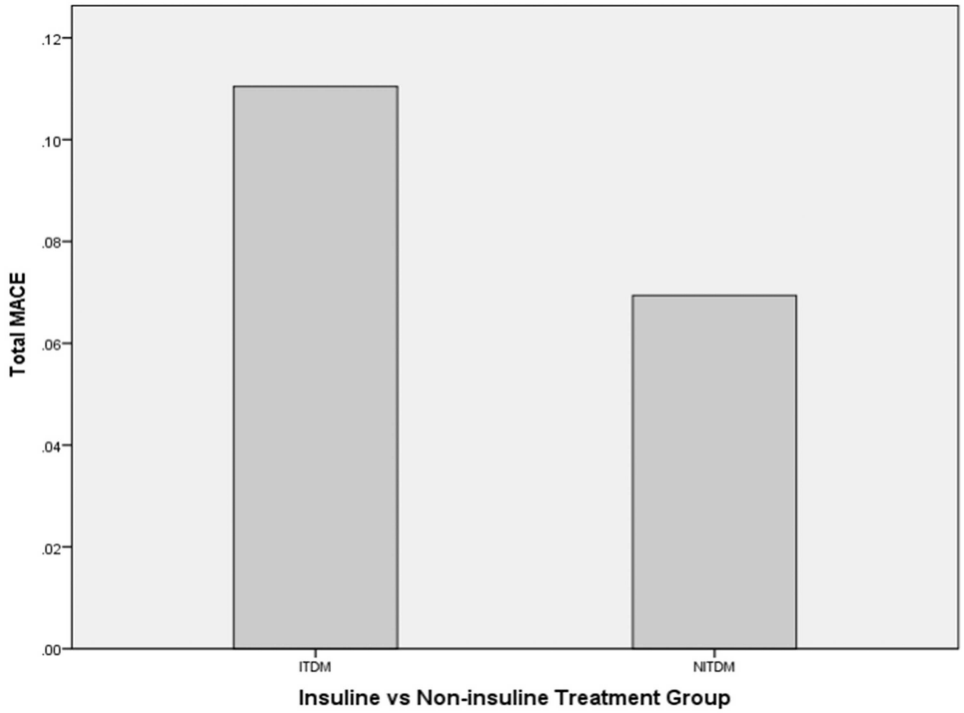

FIGURE 1 | Incidence of MACE in ITDM versus Non-ITD patients with T2DM following PCI.

TABLE 3 | Association of MACE with therapy of DM following PCI.

	Unadjusted			Adjusted		
Treatment group	**OR/HR**	**95% CI**	***p* value**	**OR/HR**	**95% CI**	***p* value**
Binary logistic regression						
Insulin treated	1.743	0.865–3.512	0.120	1.729	0.822–3.635	0.149
Non-insulin treated (ref)	1 (Ref)	—	—	1 (Ref)	—	—
Cox proportional analysis						
Insulin treated	1.695	0.874–3.284	0.118	1.554	0.793–3.045	0.199
Non-insulin treated (ref)	1 (Ref)	—	—	1 (Ref)	—	—

Note: Hazard ratio/odds ratio and 95% confidence interval by Cox proportional/binary logistic regression for MACE, unadjusted and adjusted (adjustment with [age, gender, BMI, smoking, hypertension, dyslipidemia, history of CVDs, HbA1c level, LVEF, therapy of DM, duration of DM, oral hypoglycemic, and antiplatelets]).

disease more in women than men [31, 32], our lack of gender or age-specific differences may reflect contextual variation in healthcare pathways or referral timing in Southeast Asia.

Patients receiving insulin therapy exhibited a modestly higher BMI (~1.8 kg/m^2) compared to Non-insulin users, aligning with evidence that insulin is more often prescribed to individuals with greater adiposity [33–35], though this difference was not statistically significant, possibly due to limited sample size. Income status differed significantly, with higher income in the ITDM group, consistent with literature linking socioeconomic position to therapy access [36, 37]. In Pakistan, insulin's high cost and limited production make financial capacity a determinant of access, and low health literacy is associated with poor glycemic control [38]. No statistically significant difference was observed in education level between DM therapy groups, in line with mixed evidence on its effect on glycemic control [39, 40].

LVEF, baseline hemoglobin, ECG findings, and angiographic features showed no significant differences between ITDM and Non-ITDM, consistent with studies reporting similar procedural risk profiles despite worse outcomes in ITDM [41, 42]. In our cohort, comorbid conditions such as cardiovascular disease, heart failure, peripheral artery disease, COPD, diabetic neuropathy, and prior COVID-19 infection were similarly distributed between ITDM and Non-ITDM groups. However, cerebrovascular disease was significantly more prevalent among insulin users, supporting evidence that longer diabetes duration and poor control increase stroke risk [43]. Traditional cardiovascular risk factors (smoking, hypertension, dyslipidemia, family history) were comparable, yet insulin-treated patients remain more vulnerable and require targeted secondary prevention [44–46]. ITDM patients more often received nitrate monotherapy, biguanide monotherapy, or insulin alone, whereas Non-ITDM patients more frequently received dual oral therapy. Atorvastatin was more common in ITDM, while rosuvastatin offering superior LDL-C lowering was preferred in Non-ITDM [15].

In this cohort, those receiving insulin therapy experienced a significantly higher incidence of MACE compared to those not

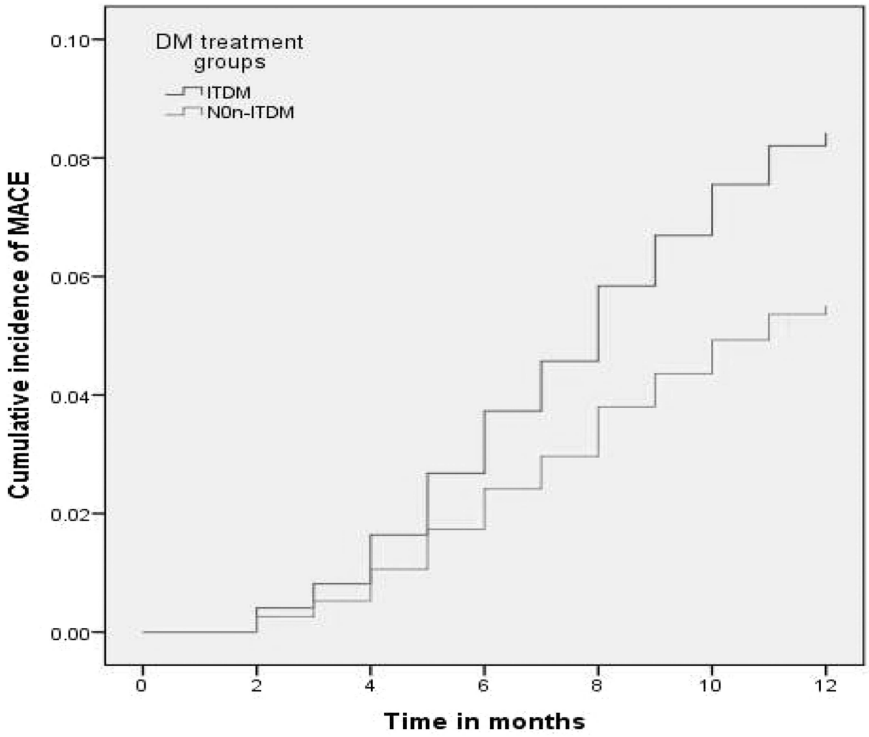

FIGURE 2 | Kaplan–Meier estimated the cumulative incidence of MACE stratified by therapy of DM.

Therapy of DM	3 months	6 months	9 months	12 months
ITDM ($n = 106$)	103	100	96	93
Non-ITDM ($n = 359$)	352	346	339	332

Values represent the number of patients at risk of MACE at each follow-up interval. Total MACE cases were 13 (12.5%) in ITDM and 27 (7.5%) in Non-ITDM patients.

on insulin therapy (12.5% vs. 7.5%). This disparity was particularly evident in the rates of stroke (3.8% vs. 1.4%) and all-cause mortality (2.9% vs. 0.8%). These higher MACE rates observed among insulin-treated patients in the present cohort are broadly consistent with trends reported in large meta-analyses, such as Bundhun et al. [27]. Although the absolute number of events was relatively low, this nearly twofold increase in MACE underscores persistent concerns surrou\nding the cardiovascular risk associated with insulin therapy in T2DM populations undergoing revascularization procedures.

Previous observational studies have consistently highlighted a link between insulin use and increased cardiovascular events, even after adjusting for glycemic control and comorbid burden. For instance, data from the UK Clinical Practice Research reported higher adjusted HR for MI, stroke, and cardiovascular death among ITDM patients compared to those on metformin monotherapy [47]. Similarly, the ORIGIN trial found that while insulin glargine improved glycemic control, it did not significantly reduce cardiovascular outcomes which raised concerns about the cardiovascular neutrality of exogenous insulin [48].

Exogenous insulin can cause short-term physiological effects such as fluid retention, sympathetic activation, and endothelial alterations, particularly in insulin-resistant patients [49]. However, there is no strong evidence that these transient effects persist or directly lead to major adverse cardiovascular events at routine therapeutic doses. Chronic hyperinsulinemia is often accompanied by central obesity, systemic inflammation, and other metabolic derangements, which themselves contribute to plaque instability and thrombogenesis [9]. Accordingly, the higher rates of repeat PCI, cerebrovascular events, and mortality (2.9% vs. 0.8%) observed among ITDM in this study are more likely to reflect advanced diabetes with beta-cell failure, vascular damage, and multiple comorbidities, rather than a direct harmful effect of insulin therapy [50, 51].

Our cohort's ITDM had significantly worse glycemic profiles, with higher RBG and HbA1c, consistent with evidence that insulin is initiated after oral therapy failure. Similar patterns have been reported globally, with insulin users often failing to meet HbA1c $\leq 7\%$ targets despite intensification [52–55]. Elevated HbA1c at PCI predicts worse outcomes, including higher MACE rates, mainly driven by repeat PCI [56]. Thus, poorer glycemic control rather than insulin itself likely explains the higher MACE incidence, with insulin use serving as a marker of cardiovascular risk. Insulin-treated patients also had a longer diabetes duration, which is strongly linked to cardiovascular risk. Studies from Denmark, China, Korea, and the UK Biobank consistently show that longer diabetes duration ($\geq$ 5–15 years) markedly increases the risk of MI, revascularization, and mortality, especially with poor control [47, 57–59]. These findings underscore that in long-standing diabetes, intensive glycemic control may not reverse and may even increase cardiovascular risk over time.

Regression and survival analyses demonstrated a high cardiovascular risk in ITDM patients post-PCI, but it was not statistically significant. In our cohort, binary logistic regression revealed that ITDM status was associated with elevated odds of experiencing MACE compared to Non-ITDM patients, with an unadjusted odds ratio (OR) of 1.743 (95% CI: 0.865–3.512; $p = 0.120$) and an adjusted OR of 1.729 (95% CI: 0.822–3.635; $p = 0.149$). Similarly, the Cox proportional hazards model, used to assess time-to-event risk over the 12-month follow-up, showed HR above 1.0 for the ITDM group (unadjusted HR = 1.695, 95% CI: 0.874–3.284, $p = 0.118$; adjusted HR = 1.554, 95% CI: 0.793–3.045, $p = 0.199$). Although these results were not significant, higher hazards observed in multiple models show a tendency of higher cumulative MACE burden in insulin-treated patients.

Several large-scale studies have shown a higher MACE risk in ITDM compared to Non-ITDM. A multicenter registry found ITDM to be an independent predictor of 12-month MACE after adjustment for clinical and procedural variables [60]. A regional cohort similarly reported markedly increased 30-day and long-term mortality in ITDM patients [61]. A systematic review of 21 observational studies confirmed higher short- and long-term risks for mortality, MI, TLR, stent thrombosis, and overall MACE in ITDM (e.g., OR 1.69 for short-term mortality, OR 1.47 for long-term MACE) [27]. One of the largest PCI registries to date also demonstrated that ITDM conferred a significantly higher adjusted hazard for 1-year MACE (HR 2.11; 95% CI 1.79–2.50), compared with non-ITDM (HR 1.27; 95% CI 1.09–1.47), both relative to non-diabetic controls. This study also demonstrated an additive risk burden through Kaplan−Meier analysis, similar to our study [15].

This study has some limitations. The relatively small sample size, low event rate, and short follow-up period may have reduced statistical power and widened CIs. Differences in baseline disease severity between groups might have influenced the results. There remains a possibility of residual confounding, as unmeasured factors including microvascular disease, systemic inflammation, central adiposity, and endothelial dysfunction, may not have been fully accounted for in the analyses. While these limitations are inherent to single-center studies with modest sample sizes, our findings still provide valuable descriptive and region-specific insights that complement existing large-scale studies, which evaluated insulin therapy and cardiovascular outcomes at a global level [27]. Despite limitations, the study clearly identifies clinical differences between ITDM and Non-ITDM patients undergoing PCI. ITDM patients had worse glycemic control, longer diabetes duration, more frequent history of stroke, and greater complication rates (e.g., repeat procedures, stroke, mortality), despite similar baseline heart function and hemoglobin levels. Furthermore, there were differences in medication patterns between the two groups, with ITDM patients being more often on atorvastatin and insulin-based regimens. These findings align with large-scale registry, cohort, and meta-analysis data showing ITDM as an independent predictor of worse cardiovascular outcomes, reinforcing the external validity of the observed trends [27].

There is a need for larger, long-term studies that track patients more closely over time. These studies should collect more detailed information about insulin use (like dosage and type), medication adherence, and other risk factors like inflammation or nerve damage. It would also be valuable to explore how patient education and self-care support (especially for those on insulin) can impact outcomes. Finally, we need clinical trials that test targeted treatments for insulin-treated patients, like the effectiveness of advanced lipid-lowering therapies or GLP-1 receptor agonists in reducing the high cardiovascular risks.

In conclusion, the direction and magnitude of effect sizes are consistent with extensive prior evidence that ITDM is associated with worse post-PCI outcomes. Insulin use likely reflects a more advanced disease state and higher overall health burden, rather than being the sole causal driver of poor prognosis. The persistent and additive risk observed across multiple large data sets underscores the clinical importance of identifying, closely monitoring, and optimizing treatment for ITDM patients undergoing PCI.

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Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Research Ethics Committee (IREC) of the Faculty of Pharmacy, University of Lahore (Ref. No: IREC-2023-5H/18-09-2023), and the Punjab Institute of Cardiology, Lahore, Pakistan (Ref. No: PH-Research-186/20-09-2023).

Consent

Every individual was informed about the purpose of the study in detail and was informed that their responses would be used solely for research purposes and would be used for publication of this research. Additionally, in compliance with ethical research standards, participants were assured of their right that, aim without any consequence, they could withdraw from study at any time. Informed consent was obtained from all the subjects involved in the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. World Health Organization, *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia* (WHO Press, 2018).

2. N. A. Bekele and J. Tadesse, "Prescription Auditing Based on World Health Organization (WHO) Prescribing Indicators: A Case of Dilla University Referral Hospital," *Journal of Drug Delivery and Therapeutics* 8, no. 6–s (2018): 21–25.

3. E. Eyth and R. Naik, *Hemoglobin A1c* (StatPearls Publishing, 2022).

4. S. Park, "Initiating Insulin Therapy in Type 2 Diabetes," *Diabetes Therapy* 14, no. 2 (2023): 401–410.

5. E. Stenberg and E. Näslund, "Major Adverse Cardiovascular Events Among Patients With Type-2 Diabetes, a Nationwide Cohort Study Comparing Primary Metabolic and Bariatric Surgery to GLP-1 Receptor Agonist Treatment," *International Journal of Obesity* 47, no. 4 (2023): 251–256.

6. C. Lundblad, "Insulin Secretion and Glycemic Control," *Diabetologia* 58, no. 10 (2015): 2020–2028.

7. D. Group, "Microvascular Outcomes of Insulin Addition," *Lancet Diabetes & Endocrinology* 10, no. 6 (2022): 321–330.

8. W. H. Herman, "Cardiovascular Effects of Insulin in Diabetes," *Current Diabetes Reports* 17, no. 10 (2017): 85–90.

9. A. D. Shah, "Insulin and Dyslipidemia in Diabetes," *Diabetic Medicine* 39, no. 3 (2022): e14765–e14770.

10. M. W. Segar, "Cardiovascular Mortality in ACCORD Trial," *New England Journal of Medicine* 382, no. 7 (2020): 599–608.

11. H. C. Gerstein, "Insulin Therapy and CVD: ORIGIN Trial Insights," *Diabetes Care* 41, no. 1 (2018): 114–120.

12. G. D. Dangas, M. E. Farkouh, L. A. Sleeper, et al., "Long-Term Outcome of PCI Versus CABG in Insulin and Non-Insulin-Treated Diabetic Patients," *Journal of the American College of Cardiology* 64, no. 12 (2014): 1189–1197.

13. S. Xu, B. Wang, W. Liu, C. Wu, and J. Huang, "The Effects of Insulin Therapy on Mortality in Diabetic Patients Undergoing Percutaneous Coronary Intervention," *Annals of Translational Medicine* 9, no. 16 (2021): 1294.

14. A. Karayiannides, S. Albugami, and D. L. Bhatt, "PCI in Patients With Diabetes: Current Perspectives," *Current Atherosclerosis Reports* 20, no. 12 (2018): 56.

15. J. Chandrasekhar, G. Dangas, U. Baber, et al., "Impact of Insulin Treated and Non-Insulin-Treated Diabetes Compared to Patients Without Diabetes on 1-Year Outcomes Following Contemporary PCI," *Catheterization and Cardiovascular Interventions* 96, no. 2 (2020): 298–308.

16. Y. Ge, D. He, Y. Shao, L. Wang, and W. Yan, "Percutaneous Coronary Intervention in Insulin-Treated Diabetic Patients: A Meta-Analysis," *Annals of Noninvasive Electrocardiology* 27, no. 5 (2022): e12953.

17. Q. Wang, H. Liu, and J. Ding, "Cardiac Versus Non-Cardiac Related Mortality Following Percutaneous Coronary Intervention in Patients With Insulin-Treated Type 2 Diabetes Mellitus: A Meta-Analysis," *Diabetes Therapy* 9, no. 3 (2018): 1335–1345.

18. T. R. Einarson, A. Acs, C. Ludwig, and U. H. Panton, "Prevalence of Cardiovascular Disease in Type 2 Diabetes: A Systematic Literature Review of Scientific Evidence From Across the World in 2007–2017," *Cardiovascular Diabetology* 17, no. 1 (2018): 83.

19. J. F. Picó-Guzmán, C. A. Salinas, and A. L. Torres, "Economic Impact of Diabetes and Cardiovascular Disease Complications in Mexico," *BMJ Global Health* 7, no. 9 (2022): e009815.

20. S. Rotonen, J. Auvinen, A. Bloigu, et al., "Long-Term Dysglycemia as a Risk Factor for Faster Cognitive Decline During Aging: A 12-Year Follow-Up Study," *Diabetes Research and Clinical Practice* 180 (2021): 109045–109052.

21. W. Hassan, "Short-and Long-Term Cardiovascular Outcomes in Insulin-Treated Versus Non-Insulin-Treated Diabetes Mellitus Patients After Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis," *Indian Heart Journal* 74, no. 1 (2022): 13–21.

22. C. E. Mendez, "Persistent Cardiovascular Risk in Insulin-Dependent Diabetes: Mechanisms and Implications," *Current Cardiology Reports* 21, no. 10 (2019): 112–119.

23. D. N. Kalkman, P. Woudstra, P. den Heijer, et al., "One Year Clinical Outcomes in Patients With Insulin-Treated Diabetes Mellitus and Non-Insulin-Treated Diabetes Mellitus Compared to Non-Diabetics After Deployment of the Bio-Engineered COMBO Stent," *International Journal of Cardiology* 226 (2017): 60–64.

24. J. A. Beckman and M. A. Creager, "Vascular Complications of Diabetes," *Circulation Research* 118, no. 11 (2016): 1771–1785.

25. J. A. Beckman, F. Paneni, F. Cosentino, and M. A. Creager, "Diabetes and Vascular Disease: Pathophysiology, Clinical Consequences, and Medical Therapy: Part II," *European Heart Journal* 34, no. 31 (2013): 2444–2452.

26. N. Li, Y.-G. Yang, and M.-H. Chen, "Comparing the Adverse Clinical Outcomes in Patients With Non-Insulin Treated Type 2 Diabetes Mellitus and Patients Without Type 2 Diabetes Mellitus Following Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis," *BMC Cardiovascular Disorders* 16, no. 1 (2016): 238.

27. P. K. Bundhun, N. Li, and M.-H. Chen, "Adverse Cardiovascular Outcomes Between Insulin-Treated and Non-Insulin Treated Diabetic Patients After Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis," *Cardiovascular Diabetology* 14, no. 1 (2015): 135.

28. Z. Kiss, G. Rokszin, Z. Abonyi-Tóth, et al., "Dissimilar Impact of Type 2 Diabetes on Cardiovascular Outcomes According to Age Categories: A Nationwide Population Study From Hungary," *Cardiovascular Diabetology* 17, no. 1 (2018): 107.

29. K. Alswat, "Impact of Gender on Type II Diabetes Glycemic and Cardiovascular Markers Control and Treatment," *Pakistan Journal of Biological Sciences* 23, no. 12 (2020): 1643–1649.

30. A. Jiménez, B. Vlacho, M. Mata-Cases, et al., "Sex and Age Significantly Modulate Cardiovascular Disease Presentation in Type 2 Diabetes: A Large Population-Based Cohort Study," *Frontiers in Endocrinology* 15 (2024): 1344007.

31. Y. Wang, "Risk Factors for Cardiovascular Events in Insulin-Requiring Diabetics," *Cardiovascular Diabetology* 18, no. 1 (2019): 73–80.

32. G. Mnatzaganian, C. Lee, G. Cowen, et al., "Sex Disparities in the Prevalence, Incidence, and Management of Diabetes Mellitus: An Australian Retrospective Primary Healthcare Study Involving 668,891 Individuals," *BMC Medicine* 22, no. 1 (2024): 475.

33. S. Erpeldinger, M. B. Rehman, C. Berkhout, et al., "Efficacy and Safety of Insulin in Type 2 Diabetes: Meta-Analysis of Randomised Controlled Trials," *BMC Endocrine Disorders* 16, no. 1 (2016): 39.

34. E. Filipova, "Effects of Pioglitazone Therapy on Blood Parameters, Weight and BMI: A Meta-Analysis," 9, no. 1 (2017): 90.

35. C. Rao, Q. Zhong, R. Wu, et al., "Impact of Body Mass Index on Long-Term Outcomes in Patients Undergoing Percutaneous Coronary Intervention Stratified by Diabetes Mellitus: A Retrospective Cohort Study," *BMC Cardiovascular Disorders* 24, no. 1 (2024): 113.

36. H. Rättö, "Socioeconomic Inequalities in Insulin Initiation Among Individuals With Type 2 Diabetes: A Quasi-Experimental Nationwide Register Study," *SSM - Population Health* 19 (2022): 101178.

37. H. Taimur, I. Ahmad, H. Khan, et al., "A Scoping Review of Type 2 Diabetes Mellitus in Pakistan Investigating the Status of Glycemic Control, Awareness, Treatment Adherence, Complications and Cost," *Frontiers in Endocrinology* 15 (2024): 1441591.

38. H. Saeed, Z. Saleem, R. Naeem, I. Shahzadi, and M. Islam, "Impact of Health Literacy on Diabetes Outcomes: A Cross-Sectional Study From Lahore, Pakistan," *Public Health* 156 (2018): 8–14.

39. X. Guo, X. Zhai, and B. Hou, "Adequacy of Health Literacy and Its Effect on Diabetes Self-Management: A Meta-Analysis," *Australian Journal of Primary Health* 26, no. 6 (2020): 458–465.

40. A. A. S. Al-Rasheedi, "The Role of Educational Level in Glycemic Control Among Patients With Type II Diabetes Mellitus," *International Journal of Health Sciences* 8, no. 2 (2014): 177–187.

41. W. Hassan, J. Saquib, M. Khatri, et al., "Short- and Long-Term Cardiovascular Outcomes in Insulin-Treated Versus Non-Insulin-Treated Diabetes Mellitus Patients After Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis," *Indian Heart Journal* 74, no. 1 (2022): 13–21.

42. Y. J. Jiang, W. X. Han, C. Gao, et al., "Comparison of Clinical Outcomes After Drug-Eluting Stent Implantation in Diabetic Versus Nondiabetic Patients in China: A Retrospective Study," *Medicine* 96, no. 17 (2017): e6647.

43. Y. B. Lee, K. Han, B. Kim, et al., "Risk of Early Mortality and Cardiovascular Disease According to the Presence of Recently Diagnosed Diabetes and Requirement for Insulin Treatment: A Nationwide Study," *Journal of Diabetes Investigation* 12, no. 10 (2021): 1855–1863.

44. M. Faghir-Ganji, N. Abdolmohammadi, M. Nikbina, et al., "Prevalence of Anemia in Patients With Diabetes Mellitus: A Systematic Review and Meta-Analysis," *Biomedical and Environmental Sciences: BES* 37, no. 1 (2024): 96–107.

45. R. Olum, F. Bongomin, M. M. Kaggwa, I. Andia-Biraro, and J. B. Baluku, "Anemia in Diabetes Mellitus in Africa: A Systematic Review and Meta-Analysis," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 15, no. 5 (2021): 102260.

46. H. Mazumder, K. F. Islam, F. Rahman, et al., "Prevalence of Anemia in Diabetes Mellitus in South Asia: A Systematic Review and Meta-Analysis," *PLoS One* 18, no. 5 (2023): e0285336.

47. F. R. Li, H. L. Yang, R. Zhou, et al., "Diabetes Duration and Glycaemic Control as Predictors of Cardiovascular Disease and Mortality," *Diabetes, Obesity and Metabolism* 23, no. 6 (2021): 1361–1370.

48. L. G. Mellbin, L. Rydén, M. C. Riddle, et al., "Does Hypoglycaemia Increase the Risk of Cardiovascular Events? A Report From the ORIGIN Trial," 34, no. 40 (2013): 3137–3144.

49. X. Tian, S. Chen, P. Wang, et al., "Insulin Resistance Mediates Obesity-Related Risk of Cardiovascular Disease: A Prospective Cohort Study," *Cardiovascular Diabetology* 21, no. 1 (2022): 289.

50. D. K. McGuire, B. Zinman, S. E. Inzucchi, et al., "Effects of Empagliflozin on First and Recurrent Clinical Events in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease: A Secondary Analysis of the EMPA-REG OUTCOME Trial," *Lancet. Diabetes & Endocrinology* 8, no. 12 (2020): 949–959.

51. S. Verma, N. R. Poulter, D. L. Bhatt, et al., "Effects of Liraglutide on Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus With or Without History of Myocardial Infarction or Stroke," *Circulation* 138, no. 25 (2018): 2884–2894.

52. H. S. Park, "Effects of Glucose-Lowering Therapy on Microvascular Complications in Diabetes," *Diabetology International* 11, no. 3 (2020): 215–222.

53. E. Skalkos, R. Rajagopal, and D. Simmons, "Diabetes Management and Outcomes Among Patients With Type 2 Diabetes Attending a Renal Service," *Journal of Diabetes Research* 2023 (2023): 1–10.

54. U. Anyanwagu, J. Mamza, R. Donnelly, and I. Idris, "Comparison of Cardiovascular and Metabolic Outcomes in People With Type 2 Diabetes on Insulin Versus Non-Insulin Glucose-Lowering Therapies (GLTs): A Systematic Review and Meta-Analysis of Clinical Trials," *Diabetes Research and Clinical Practice* 121 (2016): 69–85.

55. P. Pitak, S. Tasai, N. Kumpat, et al., "The Prevalence of Glycemic Control in Patients With Type 2 Diabetes Treated With Insulin: A Systematic Review and Meta-Analysis," *Public Health* 225 (2023): 218–228.

56. I. Dykun, S. Hendricks, O. Babinets, et al., "Hemoglobin A1c and Long-Term Mortality in Patients Undergoing Coronary Angiography: The ECAD Registry," supplement, *European Heart Journal* 43, no. S2 (2022): ehac544.

57. N. Yaliqin, S. Aimaier, D. Adi, Y. T. Ma, and Z. X. Yu, "Impact of Duration of Diabetes Mellitus on Long-Term Outcome in Type 2 Diabetic Patients With Primary Percutaneous Coronary Intervention After the First Myocardial Infarction," *Cardiology* 149, no. 4 (2024): 297–313.

58. J. Jung, S. H. Her, K. Lee, et al., "Impact of Diabetes Duration on Clinical Outcome in Patients Receiving Rotational Atherectomy in Calcified Lesions in Korea—Results From ROCK Registry," *Life* 12, no. 7 (2022): 993.

59. B. K. Benjamin, C. Qiu, Z. Han, et al., "The Association Between Type-2 Diabetes Duration and Major Adverse Cardiac Events After Percutaneous Coronary Intervention," *Journal of Diabetes Research* 2021 (2021): 1–9.

60. S. Biswas, D. Dinh, N. Andrianopoulos, et al., "Comparison of Long-Term Outcomes After Percutaneous Coronary Intervention in Patients With Insulin-Treated Versus Non-Insulin Treated Diabetes Mellitus," *American Journal of Cardiology* 148 (2021): 36–43.

61. A. Noman, K. Balasubramaniam, M. H. A. Alhous, et al., "Mortality After Percutaneous Coronary Revascularization: Prior Cardiovascular Risk Factor Control and Improved Outcomes in Patients With Diabetes Mellitus," *Catheterization and Cardiovascular Interventions* 89, no. 7 (2017): 1195–1204.