Original Article

Education Section

Coronary Angiography Findings among Diabetics and Non Diabetics Presenting with Acute Coronary Syndrome: A Case-control Study

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ABSTRACT

Introduction: Patients with type-2 diabetes are at high risk for many Cardiovascular Diseases (CVD) such as coronary artery disease, stroke, peripheral arterial disease, cardiomyopathy, and congestive heart failure.

Aim: To evaluate the coronary angiography profile in diabetics and non diabetics presenting with Acute Coronary Syndrome (ACS) in a tertiary care hospital in eastern India.

Materials and Methods: This case-control study conducted from September 2018 to October 2019 at Nil Ratan Sircar Medical College, Kolkata,West Bengal, India, comprised 200 patients (100 were diabetics and 100 were non diabetics) diagnosed with ACS based on Electrocardiography (ECG) and cardiac enzymes. Data about baseline demographic, clinical and angiographic characteristics were collected. Moreover, angiographic thrombus burden grade, Cohen and Rentrop grade for collateral circulation, and Synergy Between Percutaneous Coronary intervention with Taxus and Cardiac Surgery (SYNTAX) score were also reported.

Results: The mean number of vessel involvement was significantly higher in diabetics as opposed to non diabetics (2.1% vs. 1.5%, p-value=0.001). Left main coronary artery disease (20% vs. 10%, p-value=0.0012), ostio-proximal disease (36% vs. 20%; p-value=0.032), bi/trifurcation lesion (40% vs. 22%; p-value=0.032), diffuse disease (60% vs. 30%; p-value=0.012), chronic total occlusion (16% vs. 7%; p-value=0.008), coronary calcification (22% vs. 12%; p-value=0.04), and microvascular disease (10% vs. 4%; p-value=0.02) were significantly more frequent in diabetics compared to non diabetics. Even after thrombolysis, thrombus grade 4-5 was highly observed in diabetics than non diabetics (4% vs. 0%; p-value=0.001). Grade 3 collateral circulation was less frequently developed in diabetics than non diabetics (1% vs. 4%; p-value=0.001). High SYNTAX score was highly noticed among diabetics than non diabetics (36% vs 20%; p-value=0.03).

Conclusion: Diabetics with ACS had more thrombus burden of higher grade along with lesser collaterals, and higher SYNTAX score.

INTRODUCTION

Type-2 Diabetes Mellitus (DM) is the most prevalent complex metabolic disorder, which is approaching epidemic proportions world over and more so in developing countries like India [1]. According to the International Diabetes Federation (IDF), diabetes influences around 463 million globally and this value is projected to increase to 700 million by 2045 [2]. A close link exists between type-2 DM and CVD; CVD are the leading cause of mortality and morbidity among type-2 diabetics [3-5]. As type-2 DM is accompanied by proatherosclerotic, proinflammatory, and prothrombotic states, a number of studies have validated that type-2 diabetics historically were at a greater risk of subsequent cardiovascular events with poor clinical outcomes and higher death rates than non diabetics [6-8]. It has been reported that the peak incidence of ACS in type-2 diabetics with poor glycaemic control was much earlier as compared to non diabetics [9].

One study postulated that the risk of coronary heart disease was 1.38 times higher for each 10 year increase in the duration of type-2 DM [10]. Another study hypothesised the positive linear correlation of Haemoglobin A1c (HbA1c) and duration of type-2 DM with Gensini score, which is an important scoring system to evaluate the severity of Coronary Artery Diseases (CAD) [11]. Despite the abundance of literature on co-existence of diabetes and ACS, only a few data are available on coronary angiography profile of ACS patients with or without diabetes in India in recent years. In this context, previously published Indian literature mainly

focused on clinical presentation, risk factors, severity and extent of CVD, number of coronary vessel involvement, and mode of treatment among diabetic and non diabetic ACS patients, however no data detailing thrombus burden and collateral circulation grade among these populations exists. Hence, the present study was conceptualised with the aim to assess coronary angiography profile including thrombus burden and collateral circulation grade among diabetics and non diabetics presenting with the ACS in a tertiary care hospital in Eastern India.

MATERIALS AND METHODS

The observational, case-control study was conducted on 200 patients (100 with type-2 diabetes and 100 without diabetes), diagnosed with ACS and admitted in the tertiary care hospital, from September 2018 to October 2019 at Nil Ratan Sircar Medical College, Kolkata, West Bengal, India. This study conforms to the principles outlined in the Declaration of Helsinki and individual written consent was obtained from all participants. The study was approved by the Nil Ratan Sircar Medical College, Kolkata, West Bengal, India (Approval number NMC/767).

Inclusion criteria: Patient with previously known diabetic or first time detected diabetic by American Diabetes Association (ADA) criteria presenting with ACS were included in the case group.

Exclusion criteria: Non diabetic patients presenting with ACS were excluded (they were included in the control group for comparison).

Study Procedure

Diagnosis of ACS was confirmed based upon electrocardiography and cardiac enzymes. Firstly, all participants with ACS were treated and then were taken for coronary angiography after stabilisation. Data about baseline demographic, clinical, and angiographic characteristics were retrieved from the electronic centralised clinical database. Indications for performing coronary angiography were unstable angina, non ST segment elevation myocardial infarction, ST segment elevation myocardial infarction, and post infarct angina.

Angiographic thrombus burden was classified as follows:

- Grade 0- no thrombus;
- Grade 1- possible thrombus;
- Grade 2- the thrombus' greatest dimension is <1/2 vessel diameter;
- Grade 3- greatest dimension >1/2 to <2 vessel diameters;
- Grade 4- greatest dimension >2 vessel diameters;
- Grade 5- total vessel occlusion due to thrombus [12].

Coronary artery narrowing of 70% or greater was regarded as significant stenosis. The extension and functional capacity of coronary collateral circulation were graded using Cohen and Rentrop grading system [13]:

- Grade 0- no collaterals;
- Grade 1- side branch filling of the recipient artery without filling of the main epicardial artery;
- Grade 2- partial filling of the main epicardial recipient artery;
- Grade 3- complete filling of the main epicardial recipient artery.

The SYNTAX score was calculated by adding the individual scores for each lesion (defined as 50% luminal obstruction in vessels less than 1.5 mm). The patients were classified into tertiles according to SYNTAX score:

- Lowest SYNTAX score tertile (SYNTAX score ≤22),
- Intermediate SYNTAX score tertile (SYNTAX score of 23 to 32),
- Highest SYNTAX score tertile (SYNTAX score ≥33) [14].

STATISTICAL ANALYSIS

The data were analysed with the help of Statistical Package for Social Sciences (SPSS) version 22.0. Quantitative variables were analysed and compared using student's t-test, whereas qualitative data were analysed with chi-square test. The p-value <0.05 was reported as significant. SYNTAX score was computed with the help of an online SYNTAX score calculator [15].

RESULTS

This study was conducted on 100 ACS patients with type-2 DM, and 100 ACS patients without diabetes. The majority of the cases (80%) had long-standing type-2 DM. Most of the cases (80%) had poor glycaemic control (Glycated Haemoglobin (HbA1c) levels >7). The incidence of ACS was significantly higher in diabetics as compared to non diabetics irrespective of age group. Compared with non diabetics, the incidence of low levels of High-Density Lipoprotein Cholesterol (HDL-C) (46% vs. 20%; p-value=0.023), and high level of Triglycerides (TGs) (50% vs. 20%; p-value=0.006) were significantly higher in diabetics as compared to non diabetics. In contrast, high level of Low-Density Lipoprotein Cholesterol (LDL-C) was found to be significantly lower in diabetics than non diabetics (20% vs. 55%; p-value=0.008) [Table/Fig-1].

Angiographic parameters: The mean number of vessel involvement was significantly higher in diabetics as compared to non diabetics (2.1 vs. 1.5; p-value=0.001). Left main CAD (20% vs. 10%; p-value=0.0012, ostio-proximal disease (36% vs. 20%; p-value=0.032), bi/trifurcation lesion (40% vs. 22%; p-value=0.032), diffuse disease (60% vs 30%; p-value=0.012), Chronic Total Occlusion (CTO) (16% vs. 7%; p-value=0.008), coronary calcification (22% vs. 12%; p-value=0.04) and

Characteristics	Diabetics (n=100)	Non diabetics (n=100)	p-value
Age group (years)			
<40 years	20	8	**0.023***
40-59 years	40	20	**0.035***
>59 years	40	72	**0.042***
Clinical history			
Hypertension	46	36	**0.08***
Smoking	20	24	**0.062***
Dyslipidaemia profile			
Low high-density lipoprotein (Male: <40 mg/dL, Female: <50 mg/dL)	46	20	**0.023***
Normal high-density lipoprotein (Male: >40 mg/dL, Female: >50 mg/dL)	54	80	**0.035***
High low-density lipoprotein (>130 mg/dL)	20	55	**0.008***
Normal low-density lipoprotein (<130 mg/dL)	80	45	**0.032***
High triglycerides (>150 mg/dL)	50	20	**0.006***
Normal triglycerides (<150 mg/dL)	50	80	**0.04***

[Table/Fig-1]: Baseline characteristics among diabetics and non diabetics.
†Data are reported as percentages; *Based on Chi-square test; Bold indicates statistically significant findings (p-value <0.05); HDL: High density lipoprotein; LDL: Low density lipoprotein

microvascular disease (10% vs. 4%; p-value=0.02) were significantly more common in diabetics than non diabetics [Table/Fig-2].

Thrombus grading: As observed from the present study, 20 diabetics and 18 non diabetics were thrombolysed. Size of thrombus ranging from grade 4-5 was noticed in 20% of the diabetics even after thrombolysis compared to 0% in non diabetics. Even in non thrombolysed group, grade 4-5 thrombus grade was found to be higher in diabetics than non diabetics (50.1% vs. 9.8%) [Table/Fig-3].

Angiographic parameters	Diabetics (n=100)	Non diabetics (n=100)	p-value
Mean number of vessel involvement	2.1	1.5	**0.001#**
LMCA disease (>50%)	20	10	**0.0012***
Ostio-proximal disease (>70%)	36	20	**0.032***
Bi/trifurcation lesion	40	22	**0.032***
Diffuse disease	60	30	**0.012***
CTO	16	7	**0.008***
Calcification	22	12	**0.04***
Ectasia-aneurysm	8	5	**0.08***
Microvascular disease	10	4	**0.02***

[Table/Fig-2]: Comparison of angiographic parameters among diabetics and non diabetics.
†Data are reported as mean and percentages; #Based on student's t-test; *Based on Chi-square test; Bold indicates statistically significant finding (p-value <0.05); LMCA: Left main coronary artery; CTO: Chronic total occlusion

Thrombus grade	Thrombolysed patients			Non thrombolysed patients		
	Diabetics (n=20)	Non diabetics (n=18)	p-value	Diabetic (n=80)	Non diabetic (n=82)	p-value
Grade 0	4 (20)	10 (55.6)	**0.012***	-	10 (12.2)	**0.001***
Grade 1	0 (0)	2 (11.1)	**0.005***	10 (12.5)	10 (12.2)	**0.002***
Grade 2	4 (20)	4 (22.2)	**0.08***	10 (12.5)	46 (56.1)	**0.08**
Grade 3	8 (40)	2 (11.1)	**0.002***	20 (25)	8 (9.8)	**0.005***
Grade 4	2 (10)	-	**0.001***	25 (31.3)	4 (4.9)	**0.003***
Grade 5	2 (10)	-	**0.001***	15 (18.8)	4 (4.9)	**0.012***

[Table/Fig-3]: Comparison of thrombus grade among diabetics and non diabetics.
†Data are reported as number of patients and percentages; *Based on Chi-square test; Bold indicates statistically significant findings (p-value <0.05)

Collateral circulation grading: Grade 3 collateral circulation less frequently developed in diabetics than non diabetics (1% vs. 4%; p-value=0.001). No statistically significant differences were

observed regarding grade 0 (80% vs. 96%; p-value=0.06), grade 1 (11% vs. 0%; p-value=0.09), and grade 2 (8% vs. 5%; p-value=0.06) collateral circulation between diabetics and non diabetics [Table/Fig-4]. Comparison of grade 2 and 3 collaterals with thrombus grade 5 and CTO among diabetic and non diabetic is demonstrated in [Table/Fig-5]. This comparison suggested that exacerbation of severity was more in diabetics than in non diabetics.

Rentrop grade of collaterals	Diabetics (n=100)	Non diabetics (n=100)	p-value
Grade 0	80	91	0.06*
Grade 1	11	0	0.09*
Grade 2	8	5	0.06*
Grade 3	1	4	0.001*

[Table/Fig-4]: Comparison of angiographic grading of coronary collaterals among diabetics and non diabetics.
†Data are reported as percentages; *Based on Chi-square test; Bold indicates statistically significant finding (p-value <0.05)

Parameters	Diabetics n (%)	Non diabetics n (%)	p-value
CTO (n=23)			
CTO with no collaterals	10 (43.5)	1 (4.3)	0.003*
CTO with grade 2,3 collaterals	6 (26.1)	6 (26.1)	0.03*
Grade 5 thrombus (n=21)			
Grade 5 thrombus with no collaterals	14 (66.7)	1 (4.8)	0.002*
Grade 5 thrombus with grade 2, 3 collaterals	3 (14.3)	3 (14.3)	0.03*

[Table/Fig-5]: Comparison of grade 2 and 3 collaterals with grade 5 thrombus and chronic total occlusion among diabetics and non diabetics.
†Data are reported as number of patients and percentages. *Based on Chi-square test. Bold indicates statistically significant finding (p-value <0.05); CTO: Chronic total occlusion

SYNTAX score: High SYNTAX score was statistically more prevalent among diabetics than non diabetics (36% vs. 20%; p-value=0.03). Even low SYNTAX score is less prevalent among non diabetics as compared to diabetics (24% vs. 45%; p-value=0.012) [Table/Fig-6].
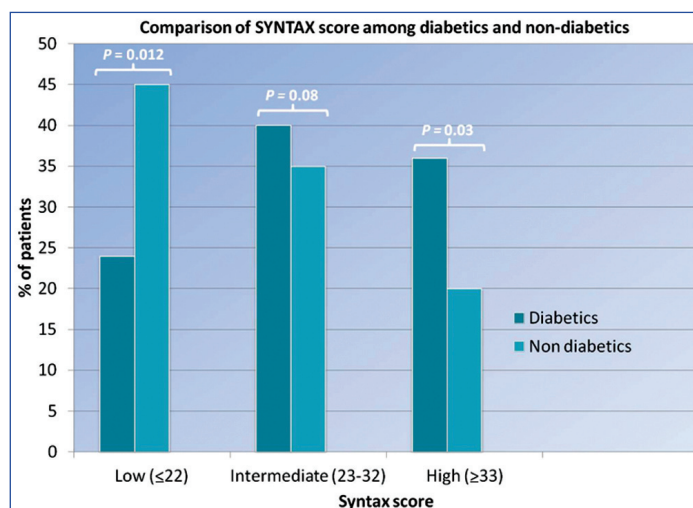
[Table/Fig-6]: Graph showing comparison of SYNTAX score among diabetics and non diabetics.

DISCUSSION

Type-2 DM is a major health concern in India due to direct cause of death and increases the risk of other diseases including CVD [16]. Endothelial dysfunction is a consequence of type-2 DM, and particularly, it is associated with several pathogenic mechanisms, including reduced nitric oxide production, anticoagulant properties, increased platelet aggregation, increased expression of adhesion molecules, increased expression of chemokines and cytokines, and increased reactive oxygen species production from the endothelium [17]. These mechanisms play crucial role in the progression of diabetic vascular complications comprising atherosclerosis and other vascular pathologies. Thus, endothelial dysfunction can develop several types of CVD such as myocardial infarction, peripheral vascular disease, ischaemic stroke, and others. Herein, coronary angiography findings among diabetics and non diabetics presenting with ACS were compared.

Diabetic dyslipidaemia is a cluster of lipoprotein abnormalities that comprises the triad of elevated TGs levels, reduced HDL-C levels and a preponderance of small dense LDL-C particles [18,19]. All three elements of this atherogenic dyslipidaemia triad are associated with atherogenesis and increased risk of CVD [20,21]. As well, smoking and hypertension are important causative agents in developing type-2 DM as well as CVD.

The present study demonstrated higher mean vessel involvement in diabetics than in non diabetics (2.1 vs. 1.5; p-value=0.001). This finding was correlated well with the finding of Bharath S et al., wherein mean vessel involvement in diabetics and non diabetics were 1.81 and 1.59, respectively. Consistent with the findings of Shah T, findings of the present study also demonstrated that diabetics had significant CTO, calcification, and diffuse disease than non diabetics [22,23]. Collectively, it has been concluded that angiography parameter was worsened in diabetics as compared to non diabetics.

The extent of collateral filling on angiography is the most important determinant of the severity of myocardial damage and mortality following coronary artery occlusion. The high collateral grade indicates good collateral circulation i.e. protective effects towards a favourable functional outcome. Type-2 DM impairs collateral vessel growth by multiple mechanisms [24]. The present study revealed that grade 3 collateral circulation was less commonly developed in diabetics as compared to non diabetics (1% vs. 4%; p-value=0.001). In the present study, even after thrombolysis, the size of thrombus was increased in diabetics than non diabetics. This indicated that diabetics had more resistant thrombus than non diabetics. As well, the authors in this study, compared SYNTAX score between diabetics and non diabetics. A high SYNTAX score is suggestive of complex conditions and represents the greatest risks to patients undergoing percutaneous coronary intervention. The most significant observation of the present study is that diabetics appeared to have higher SYNTAX score than non diabetics (36% vs. 20%; p-value=0.03) and low SYNTAX score was less prevalent among non diabetics than diabetics (24% vs. 45%; p-value=0.012). Correspondingly, based on his recent work, Shah T concluded that diabetics had higher syntax score; for score of ≥33, 9% were diabetics while 1% were non diabetics and for score of 0-22, 61% diabetics than non diabetics have 86% [23]. As expected, these existing findings hypothesised that diabetics have more severe angiographic-proven coronary artery disease than non diabetics. Also, diabetics have more likelihood to develop diffuse and extensive coronary atherosclerosis [25].

Limitation(s)

The present study is limited by relatively small sample size. Taking into account the size of the Indian population, prevalence rates mentioned in this report may not be a true representation of the entire population because of the single centre study design. Also, intravascular ultrasound was not performed for the assessment of left main coronary artery and left anterior descending ostio-proximal lesions. More studies with robust designs representing all parts of the country are warranted.

CONCLUSION(S)

Diabetics had more severe form of ACS than non diabetics as evident from the results of the present study. Diabetics had more thrombus burden of higher grade, lesser collaterals, and higher SYNTAX scores. Not only earlier diagnosis of type-2 DM with strict glycaemic control but also control of hypertension, smoking and dyslipidaemia might decrease the coronary atherosclerotic disease burden among diabetics.

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