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Original Research Article

Diabetic CAD versus non diabetic CAD: a comparative study of clinical features, risk factors and angiographic profile

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ABSTRACT

Background: Current study was conducted to compare clinical, risk factor profile and angiographic features of diabetic and non diabetic patients with coronary artery disease.
Methods: This case control study was carried out in 142 patients, who had angiographically proven CAD. 71 patients with diabetes or newly detected with diabetes constituted the cases and remaining controls. Necessary data was collected. Standard statistical analytics were used and risk factor and investigatory profile, including ECG, 2D ECHO and coronary angiography were compared between diabetic and non diabetic CAD patients.
Results: Mean age of occurrence of CAD was 52.15±6.81, with no significant difference in mean age among groups. Higher prevalence of CAD was seen in female diabetics. Hypertension, dyslipidaemia, obesity and smoking were found as major risk factors of CAD. Atypical chest pain and silent ischemia were most common among diabetic CAD. Multiple vessel involvement (47.9% vs. 18.3%, p <0.01) is more common in diabetics. Prolonged duration of diabetes and poor glycemic control were associated with more severe and extensive form of CAD (p<0.05) and the treatment outcome in the form of CABG (p<0.01).
Conclusions: Diabetic CAD patients were more likely to have severe, extensive coronary artery involvement. Significant number of diabetics had asymptomatic ischemia, with normal ECG and 2D echo, emphasizing the need of extensive cardiac evaluation at an early stage. Hypertension, dyslipidaemia, female gender along with uncontrolled and prolonged duration of diabetes, caused more critical form of CAD and poor treatment outcomes in the form of CABG.

Keywords: Coronary artery disease, Coronary Angiography, Diabetes

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders, due to relative or absolute lack of insulin, resulting in elevated blood glucose levels in association with long term vascular complications.[1-3] Diabetes mellitus is the second most common disease worldwide ranking next to cardiovascular disorder. The current estimation shows that there are 3.5 crore persons with diabetes in India and this number is likely to raise up to 5.72 crores by 2025. India has now been declared by WHO as the "diabetes capital of the world".[2] Cardiac affliction is by far the commonest cause of mortality in patients with diabetes.[4] Diabetes has become predominantly a disease of the cardiovascular system and hence

cardio-diabetology is fast emerging as subspecialty throughout the world to tackle the menace of cardiac related mortality and morbidity in diabetes particularly in type 2 DM.[5] Major differences were observed in clinical features, risk factor profile and most importantly CAD characteristics on angiography between diabetic and non diabetic patients in literature review. The cause of this difference in the diabetic population is not well understood. To date very few studies, had recorded these differences between diabetic and non diabetic patients in our country. Thus this study was designed to focus on risk factors, clinical presentation and angiographic characteristics of coronary artery disease in diabetic patients compared with that of non diabetic patients in a tertiary care centre.

METHODS

The present study was an observational case control study, which was geared around the coronary artery disease patients. After obtaining approval from institute ethics committee, study was conducted in departments of medicine and cardiology, SBKSMIRC, a tertiary care centre for a period of 2 years, starting from November 2017 to October 2019. Patients who underwent coronary angiography and diagnosed to be having CAD were enrolled in the study after taking written informed consent. A total of 142 patients were enrolled of which 71 patients with diabetes formed the cases group and the remaining 71 patients were taken as controls as per inclusion and exclusion criterias laid down.

Inclusion criteria

Inclusion criteria for current study were; case: (CAD patients who are diabetic): previously known diabetic or first time detected diabetic by American diabetic association (ADA) criteria and having coronary artery disease. Control: (CAD patients who are non- diabetic): diagnosed as having coronary artery disease who are non diabetic or not fulfilling ADA criteria

Exclusion criteria

Exclusion criteria for current study were; age <18 years and >60 years, any person who was not willing to participate in study.

Procedure

Detailed history with main focus on clinical features, risk factor and clinical examination was done. Necessary lab investigations like CBC, RFT, electrolytes, were done. HbA1C levels were done in cases group. Cardiac specific investigations like ECG, 2D ECHO were done in all the patients. All the findings, including those of coronary angiography, were noted down in preformed CRF and appropriate data collected after the study was compiled in MS office excel. Then data analysis was done by statistical software. Descriptive statistics, Odds ratio, Chi Square test and regression analysis were applied for analysis and important correlations and conclusions were drawn.

RESULTS

In the present study, the mean age of the whole study group was 52.15±6.81 years. As age is increasing there is more occurence of CAD among both the groups, with slightly higher but, stastically insignificant proportion in diabetic group (70.4% vs 54.9%, in age group 51-60 years). The Male: Female ratio of the total study group is 2.8:1. Out of 71 diabetic patients, 33.8% were females, with Male: Female ratio being 2:1, whereas in non diabetics only 18.31% were females with male: female ratio being 4.5:1. On evaluation of clinical presentation among all the CAD patients, we found that Chest pain is the most common presenting feature, followed by palpitations, breathlessness, and perspiration in decreasing frequency. 20% of diabetic patients had no chest pain at all, which is a very significant observation (p=0.004) and there is almost equal incidence of typical and atypical location of chest pain, with slightly more diffuse in location (36.84%) among diabetic patients (p=0.029).

Prevalence of hypertension is more in diabetic CAD patients, as compared to non diabetics (42.2% vs. 23.9%, p=0.02) (Table 1). Similar finding was observed with dyslipidaemia, which was more in diabetics (82% vs. 63%, p=0.02). When individual lipid values were analysed we found that mean values of serum cholesterol were within normal range in both the groups, but higher in diabetic patients. Serum triglycerides and serum LDL were on higher side in diabetic patients compared to non diabetic group. Mixed dyslipidemia is present in the form of raised triglycerides and LDL was most common type among diabetics constituting 40.9%. Prevalence of obesity and smoking was less in diabetic CAD patients when compared to non-diabetics, with following comparisions respectively (15.5% vs. 47.9%, p<0.01), (32.4% vs. 63%, p<0.01). The mean values of fasting blood sugar, Post prandial blood sugar and glycosylated Hemoglobin were 161.25±35.29, 233.39±57.19 and 10.05±1.67 respectively, suggesting uncontrolled hyperglycemia. All 71 patients with diabetes had a HbA1C values more than 7.0, (Table 7), 14 patients (19.7%) had fair glycemic control , 35 patients (49.3%) had poor glycemic control and 22 patients had very poor glycemic control or uncontrolled hyperglycemia. A significant number of diabetic patients had normal ECG compared to non diabetics (28.1% vs. 12.6 %, p=0.02) (Table 2). When important 2D echo findings (Table 3) were compared among the groups, we found, that a significantly less number of diabetic CADs had RWMA (57.74% vs. 87.32%, p<0.01). Very less number of diabetic CADs had poor LVEF <40% indicating the systolic dysfunction is very less among diabetics (28% vs 53%, p <0.01).

Table 1: Distribution of risk factors among case and control group.

Risk Factor	Groups	Diabetics N (%)	Non diabetics N (%)	P value
Hypertension	Present	30 (42.25)	17 (23.94)	0.02
	Absent	41 (57.75)	54 (76.06)	
Obesity	Normal (BMI: 18-23)	31 (43.66)	13 (18.30)	<0.01
	Over weight (BMI: 23-25)	29 (40.84)	24 (33.81)	
	Obese (BMI: >25)	11 (15.50)	34 (47.89)	
Addiction	No addictions	23 (32.40)	3 (4.22)	<0.01
	Smoker	23 (32.40)	44 (61.99)	
	Alcoholic	5 (7.04)	4 (5.63)	
	Tobacco chewer	8 (11.26)	3 (4.22)	
Dyslipidemia	Present	58 (81.70)	45 (63.38)	0.02
	Absent	13 (18.30)	26 (36.62)	

Table 2: ECG findings, (n=71).

ECG	Diabetics, N (%)	Non diabetics, N (%)	P value
Normal	20 (28.2)	9 (12.68)	0.02
Abnormal	51 (71.8)	62 (87.32)	

Table 3: 2D ECHO findings, (n=71).

2D ECHO findings	Group	Diabetics N (%)	Non diabetics N (%)	P value
RWMA	Present	41 (57.74)	62 (87.32)	<0.01
	Absent	30 (42.26)	9 (12.67)	
LVEF	>40%	59 (83.10)	33 (46.48)	<0.01
	<40%	12 (16.90)	38 (53.52)	
Diastolic dysfunction	Present	51 (71.8)	34 (47.89)	<0.01
	Absent	20 (28.17)	37 (52.11)	

Table 4: Lesion on coronary angiography, (n=71).

CAG	Group		P value
	Diabetics N (%)	Non diabetics N (%)	
Small vessel disease	1 (1.4)	3 (18.3)	<0.01
SVD	13 (18.3)	35 (49.2)	
DVD	23 (32.4)	20 (28.2)	
TVD	34 (47.9)	13 (18.3)	

Diastolic dyfuntion, the most common cardiac sabnormality in diabetics CAD, present in almost three fourth of them. (71.83% vs. 47%, p<0.01). As shown in (Table 4), triple vessel disease (TVD) is quite high in diabetic patients, when compared with those in non-diabetic group (47.9% vs. 18.3%, p<0.01). Significantly high percentage (47.89%) of diabetic patients had total occlusion of minimum one vessel. In non-diabetic group there is almost equal distribution of subjects in terms of severity of stenosis of the vessel, with slightly higher proportion of them had mild and moderate stenosis (Table 5).

Table 5: %stenosis of vessel on CAG, (n=71).

% Stenosis on CAG	Group		P value
	Diabetics N (%)	Non diabetics N (%)	
70-95% (Mild and moderate)	10 (14.08)	27 (35.03)	0.01
96-99% (Severe)	27 (38.03)	21 (29.57)	
100% (Total occlusion)	34 (47.89)	23 (32.39)	

Among diabetic CAD patients, 8 patients were newly detected for diabetes and of them 62.5% patients had SVD and 50% had severe stenosis of coronaries. 29 patients had history of diabetes for more than 10 years, in which 75.8% had TVD and 68.9% had very severe stenosis in form of total occlusion of vessel (Table 6). 81.8% of the patients having severely derranged HbA1C (>11), had TVD and 63% had total occlusion of vessel (Table 7). In patients with poor glycemic control (HbA1C > 8.5), 57.9% had TVD and 56.1% had total occlusion. In fairly controlled diabetic group (HbA1C 7.1-8.5), only 7.14% had TVD, but 57.1% had SVD and 50% had severe stenosis. Correlation of severity of hyperglycemia with severity of CAD was statistically significant (p<0.01).

Almost half of the diabetic CAD (49.3%) had CABG as treatment outcome, whereas many of the non diabetic CAD (59.1%) were advised for medical management (p<0.01) (Table 8). 58.4% of the patients whose treatment outcome is medical management had fair glycemic control. 70.8% of those who underwent PTCA had poor glycemic control. A total of 35 diabetic patients were advised CABG out of which 97.1% had poor or very poor glycemic control (Figure 1). When duration of diabetes was correlated with the treatment outcome (Figure 2), we found that 60 % of those who were adviced for CABG had diabetes for more than 10 years.

Table 6: Correlation of duration of diabetes and type and severity of lesion on CAG.

Duration of diabetes (years)	Total	Lesion on coronary angiography				P value	Severity of stenosis on CAG			P value
		Small vessel disease	SVD	DVD	TVD		70-95%	96-99%	100%	
Newly detected	8	0 (0)	5 (62.5)	2 (25)	1 (12.5)	0.01	4 (50)	3 (37.5)	1 (12.5)	0.02
0-5	11	0 (0)	4 (36.4)	5 (45.4)	2 (18.2)		3 (27.3)	3 (27.3)	5 (45.4)	
5-10	23	1 (4.3)	3 (13.0)	10 (43.5)	9 (39.2)		2 (8.7)	13 (56.5)	8 (34.8)	
>10	29	0 (0)	1 (3.4)	6 (20.7)	22 (75.9)		1 (3.45)	8 (27.6)	20 (68.9)	

Table 7: Correlation between glycemic control and type and severity of lesion on CAG.

Glycemic control (HbA1C)	Total	Lesion on coronary angiography				P value	Severity of stenosis on CAG			P value
		Small vessel disease	SVD	DVD	TVD		70-95%	96-99%	100%	
Fair (7.1- 8.5)	14	1 (7.1)	8 (57.1)	4 (28.7)	1 (7.1)	<0.01	5 (35.7)	7 (50)	2 (14.3)	0.02
Poor (8.6 -11.0)	35	0 (0)	4 (11.4)	16 (45.7)	15 (42.9)		4 (11.4)	13 (37.1)	18 (51.5)	
Very poor (>11.0)	22	0 (0)	1 (4.5)	3 (13.6)	18 (81.9)		1 (4.5)	7 (31.8)	14 (63.7)	

Table 8: Comparison of treatment outcome in diabetic and non diabetic CAD, (n=71).

Treatment outcome	Diabetics	Non Diabetics	P value
Medical management	12 (16.9)	42 (59.1)	< 0.01
PTCA	24 (33.8)	16 (22.5)	
CABG	35 (49.3)	13 (18.4)	

DISCUSSION

Coronary artery disease (CAD) accounts for the major chunk of mortality in diabetes. Diabetes mellitus (DM) is a well-established risk factor for development of coronary artery disease (CAD). Incidence of heart diseases & associated mortality was shown to be 4 times higher in people with type-2 DM. Coronary artery disease in diabetics differ in many ways from non diabetics, in form of more severe and extensive coronary vessel involvement. The prevalence of CAD increases as age advances. Most of the studies we reviewed also had similar findings, of average age of occurrence of CAD around 55 years.[6-10] Mean age of our study group was 52.15±6.81 years, which was almost nearer. Early occurrence of CAD by a minimum of a decade in diabetic patients is a known fact. But in contrary to this fact, in our study mean age of diabetic and non diabetic patients were almost similar and few other studies also showed no age difference in the occurrence of CAD among diabetics and non diabetics.[7-13] When gender ratio was compared between diabetic and non diabetic CAD groups, we found a major difference. In non diabetic CAD study population, male predominance in occurrence of CAD was found, ratio being 4.5:1. But this ratio was drastically reduced to 2:1 in diabetic CAD patients, suggesting that females with diabetes are more prone to develop CAD, compared with their counterparts in non diabetic group and this observation is well comparable with other studies.[6,14] This wide gender difference in the present study may be due the fact that in females there were

several negative potential factors that influence the stability of glycemic control like use of hormonal contraception, menstrual variability in glucose control and insulin sensitivity, pregnancy, and variability of glucose control through perimenopause.[13]

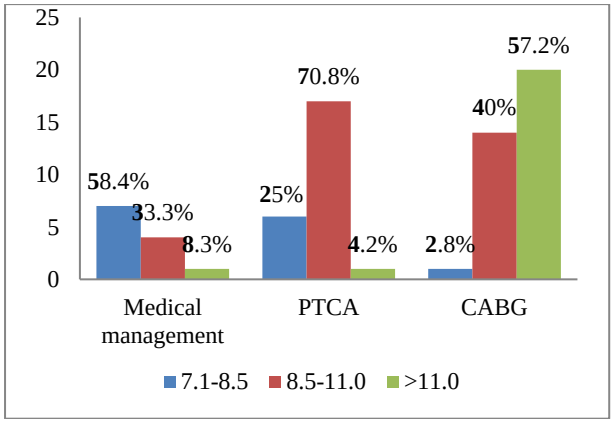

Figure 1: Treatment outcome and glycemic control.

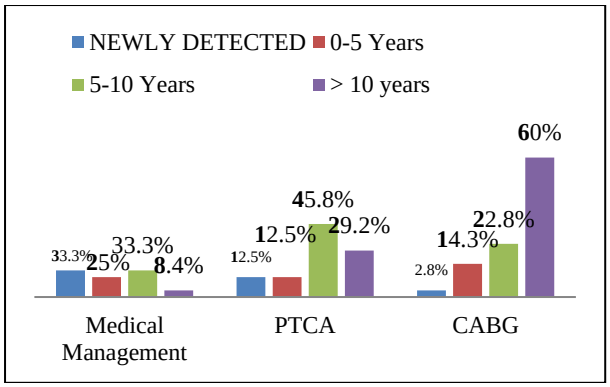

Figure 2: Treatment outcome and duration of diabetes.

According to the Framingham heart study, the traditional and established modifiable risk factors of coronary artery disease were hypertension, obesity, diet, sedentary lifestyle, dyslipidemia, and smoking. In our study we found hypertension, dyslipidemia, obesity and smoking as major risk factors in patients with coronary artery disease. In the present study, hypertension is more prevalent among diabetic CAD when compared to non diabetics (42.2% vs. 23.9%, p-value: 0.02). Many other studies also showed higher prevalence of hypertension among diabetic CAD.[6,7,11,15,16] On searching the literature, we found a renowned entity called diabetic dyslipidemia, where in there is a combination of raised triglycerides and LDL cholesterol and decreased HDL cholesterol in diabetic patients. Study done by Pandya et al in the same geographical area on the prevalence and pattern of dyslipidemia among type 2 diabetes, found very high prevalence (82.9%) of diabetic dyslipidemia and having mixed pattern of dyslipidemia, with most of them having a raised triglycerides and LDL cholesterol levels.[17] In our study 82% of diabetic CADs were dyslipidemic. Though the prevalence of dyslipidemia is quite less in non diabetics compared to diabetics, still it is significant (63%). This finding suggests an independent role of dyslipidemia in causation of CAD. Other studies also found similar observation.[10,11,18,19] Obesity is an important and well established risk factor for CAD. Also obesity is a major risk factor for diabetes with causative implication by increasing insulin resistance. But to our surprise, we got a contrary finding that prevalence of obesity is quite low in diabetic than non diabetic CAD (56.3% vs. 81%). We could not find such comparable results in literature search. Such finding may be due to small number of study population, which might not be representative of general population. Similar result was obtained for other important and well established risk factor of CAD, smoking. Percentage of smokers was less in the diabetic CAD group compared to non diabetics. (32.4% vs. 64%). In a study conducted by Parvin et al they found that proportion of smokers in diabetic CAD is much lesser than those in nondiabetic group with CAD (42% vs. 67%).[17] Similar finding was obtained in many of the similar studies conducted.[15,16,18] On correlating various risk factors of CAD along with diabetes and causation of severe lesion on angiography, we found that non modifiable risk factors like advancing age , female gender and modifiable risk factors like hypertension, dyslipidemia leads to more severe lesion in diabetic CAD. Chest pain is the most common presenting symptom of the coronary artery disease. In our study, the chest pain is atypical, mild and diffuse in nature among many of the diabetics (68.4% vs. 8.8 %) . Also, we found that about one fifth of diabetic patients had no chest pain (silent ischemia) at all, which is a significant finding (p=0.004). Very few studies were conducted regarding silent myocardial infarction in diabetics, and one such study conducted by Hernandez et al, in 2011 found that silent myocardial infarction was detected in 21.9% of diabetic patients.[20,21] Electrocardiography (ECG) is considered to be inexpensive screening tool and frequently used first line diagnostic tool in detecting coronary artery disease especially ACS. But recent evidences suggest that usefulness of ECG as screening tool is less in patients with diabetes. In our study we found that more than 25% of CAG confirmed CAD patients with diabetes were having normal ECG. So these are the potential group of patients, who might be missed if we use only ECG as screening tool for detection of CAD especially in diabetics. On 2D Echocardiography, Left ventricular diastolic dysfunction is more pronounced than left ventricular systolic dysfunction in diabetics when compared to non diabetics, (71.83 % vs 48%, p<0.01). Boyer et al and Poirier in their studies also found the similar findings.[21,22] On comparative analysis of CAG features of diabetic and non diabetic CAD patients,Multiple vessel or triple vessel involvement is more pronounced in diabetic patients, when compared with those in non diabetic group (47.9% vs. 18.3%) and this finding is statistically very significant (p=0.0004). Our findings were well comparable to most of the studies conducted in this area of interest when severity of vessel occlusion was compared, diabetic CAD had more of total

vessel occlusions than mild and moderate stenosis (47.9% vs. 14%), whereas in non diabetic group there was almost equal distribution, with slightly high proportion of mild stenosis.[6,7,9,10,12,23-26] Similar findings were observed in various studies conducted comparing severity of stenosis among diabetics and non diabetics.[24,27-29] On subgroup analysis of only diabetic CAD patients (N=71) we found, 11.2% prevalence of CAD at the time of diagnosing diabetes. In this newly detected diabetes group, a significantly high percentage (62.5%) had single vessel disease, and 50 % had mild to moderate stenosis of vessel. Though the number of patients was very small to derive any conclusions, it definitely requires large sample population based studies to find out prevalence of asymptomatic CAD in prediabetic and early stages of diabetes. As the duration of diabetes increases, there is more worse angiographic findings in terms of more number of vessel involvement and more severe stenosis. Most of the studies done in this area of interest also showed similar findings.[12,23-26] The reason for this more severe and extensive lesion on CAG in long standing diabetic patients may be due to increased atherogenesis and plaque formation.

Poor glycaemic control was also found to be risk factor for severe CAD in our study. In poor glycaemic control patients, there is more of multi vessel involvement and also severe stenosis of vessel. In group with HbA1C levels greater then 11.0, mostly had triple vessel involvement and total occlusion of the vessel, requiring immediate intervention. The reason may be due to the fact that prolonged and uncontrolled hyperglycemia causes more rapid and increased athererogenesis. Our results are comparable with studies conducted by Hegde et al and Malthesh et al.[6,25] As far as the treatment outcome of our study group is concerned most of the diabetic CAD patients were advised to undergo CABG and this observation is well correlated with poor glycaemic control and prolonged duration of diabetes, whereas most of the non diabetic CAD patients were advised for adequate medical management followed by staged interventions.

Limitations

Limitations of current study were; patients aged greater than 60 years age were excluded from the study, to reduce the confounding effect of old age on CAD occurrence, more advanced scoring systems for quantifying angiographic lesions like Syntax score, Gensini scoring were not used in the present study due to technical non availability in our institute and the present study was a single centered study.

CONCLUSION

Diabetes is considered as CAD risk equivalent and cardio-diabetology is a fast emerging sub speciality throughout the world to tackle the menance of cardiac related mortality and morbidity in diabetics. Silent CAD and normal ECG were prevalent in significant number of diabetics, emphasizing the need of early and extensive cardiac evaluation in diabetic patients. Hypertension, dyslipidemia and female gender along with diabetes causes worse CAD, reiterating the importance of more integrated approach in following a diabetic patient. Prolonged duration of diabetes and poor glycemic control were associated with severe and extensive coronary artery involvement and also poor outcome in the form of CABG, enunciating the need for strict glycemic control in diabetic patients.

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