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ANGIOGRAPHIC COMPARISON OF EXTENT AND SEVERITY OF CORONARY ARTERY DISEASE BETWEEN DIABETIC AND NON DIABETIC PATIENTS

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ABSTRACT

Objective: To compare the severity and extent of coronary artery disease in type-2 diabetic and non-diabetic patients suffering from coronary artery disease.

Methodology: This cross sectional study was conducted at National Institute of Cardiovascular Disease, Karachi (NICVD) from 8th December 2005 to 7th June 2006. Non probability convenience sampling was used. All patients with suspected or known coronary artery disease who were planned for angiography and revascularization were included. Patient with previous percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG), known valvular heart disease and type 1 diabetics were excluded from study. Patients angiograms were evaluated for lesions in coronary arteries, number of vessel involved and type of lesions.

Results: It was found that diabetic patients are more prone to severe disease in each coronary artery. In diabetic patients severe disease was significantly higher in LAD (54.7% vs. 44%, $p < 0.01$), RCA (61.3% vs. 36 %, $p < 0.002$) and Left Circumflex (60% vs. 36%, $p < 0.003$). Diabetic patients were found to have more extensive disease as compared to non diabetics, so multi vessel disease was more common in diabetics as compared to non diabetics (54.7% vs. 21.3 %, $p < 0.001$) . It was found that Type C lesions were more common in diabetics (32.7% vs. 14.9 %, $p < 0.001$). Diabetic patients were having more severe, multivessel and diffuse disease as compared to non diabetics.

Conclusion: Coronary artery disease is more aggressive in diabetic patients usually involving more vessels, diffuse in nature, more severe and having more complicated lesions.

Key Words: Percutaneous Coronary Intervention, Coronary Artery Bypass Graft, Left Anterior Descending Artery, Right Coronary Artery, Left Circumflex Artery, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes mellitus affects a large number of population in the world, and is associated with several complications, which impair quality of life and causing a large economic burden on society. The prevalence of diabetes for all age groups worldwide was 2.8% in 2000 and it is estimated that this will become 4.4% in 2030. So the total number of people with diabetes will be increase from 171 million in 2000 to 366 million in 2030.[1] In Pakistan the prevalence of diabetes mellitus is about 5.3% to 16.2%.[2]

Cardiovascular diseases are the major cause of death among patients with diabetes mellitus.[3] Large epidemiological studies such as the Framingham study have identified diabetes mellitus is one of the most important independent risk factors for CAD, but now diabetes mellitus is considered as CAD risk equivalent.[4] So, a diabetic person without clinical events of CAD has the same future risk for angina pectoris, MI as a person with known CAD.[5] Mortality due to CAD has declined by about 60% during the past 20 years. Unfortunately, this positive tendency in CAD mortality in the non-diabetic population does not apply to the diabetic cohort. In the USA during the past 30 years, non-diabetic men experienced a 44% decline in age- adjusted mortality due to CAD compared to only 17% in diabetic men. Mortality in non-diabetic women fell 20%, but simultaneously increased 11% in diabetic women.[6]

The prevalence of CAD in adult population without diabetes mellitus is 2% to 4%, but this is increased to 55% in adult diabetic cohort. In diabetic adult men the cardiovascular mortality rate is more than double and more than quadrupled in women compared with non-diabetes counter parts.[7] The prevalence of CAD in the world is less in women compared to men below 60 years of age. But in Pakistan, the prevalence of CAD in men and women is about equal in urban population. The overall prevalence of CAD in urban population of Pakistan is 26.9%, of which 23.7% in men and 30.0% in women. One in four middle aged adults in urban population of Pakistan has prevalent CAD. This prevalence of CAD in adult population is the highest one as compared to the rest of the world.[8] The prevalence of CAD in rural areas of Pakistan is about 11.2%. The prevalence in women is high (13.3%) compared to men (7.9%).[9]

Even though the increased risk for CAD in the diabetic population is well recognized, but less data exist for the factors that determine the severity and extent of CAD and its anatomical distribution in the human coronary tree in different populations.[10] The severity and extent of CAD in diabetic patients compared with non-diabetic subjects is controversial, although some data show a more diffuse and distally located coronary atherosclerosis in diabetic patients.[11]

The aim of this study is to know the extent and severity of coronary lesion in diabetics to emphasize on more aggressive primary prevention studies in diabetic population as most of these lesions are diffuse and distal and interventional options are less successful as compared to non diabetics.

METHODOLOGY

This cross sectional study was conducted in national institute of cardiovascular disease Karachi (NICVD). Non probability convenience sampling was used. Data was collected for 6 months from 8th December, 2005 to 7th June, 2006. All patients with suspected or known coronary artery disease from age 25 to 75 were included in the study whom were planned for angiography and revascularization. Patients were selected on the basis of angina pectoris refractory to medical treatment being considered for revascularization, patients with signs of ischemia on non-invasive testing, patients of post myocardial infarction status having angina pectoris, or non invasive evidence of left ventricular systolic dysfunction, and signs of ischemia after stress test were included in this study. Patient with previous percutanous coronary intervention (PCI) and coronary artery bypass graft (CABG), known valvular heart disease and type 1 diabetics were excluded from study. Detail history of patients was taken and recorded on pre designed proforma. Patient interviewed for diabetics mellitus, hypertension, dyslipidemia, family history of ischemic heart disease and cigarette smoking. After complete explanation about the procedure a written informed consent was taken from the patient or close relative. Patients were kept in fasting state for four to six hours. The coronary angiographies were carried out by different cardiac physicians but the angiographic technique was uniform during the study period. The coronary angiography was done by Seldinger technique (right femoral artery approach) under strict aseptic precautions. Diabetes defined in this study when there was history of diabetes or patient on some antidiabetic treatment or fasting blood sugar level was more than 125mg/dl at more than one occasion. The right coronary artery was divided into three segments: proximal (extending from the ostium halfway to the acute margin), middle (between the proximal and distal segments), and distal (extending from the acute marginal to the origin of the posterior descending artery).The left main coronary artery, which extends to the bifurcation of the left anterior descending and circumflex arteries, was easily identified. The left anterior descending artery was divided into three segments, with proximal segment , extending to the first visible septal perforator. Mid LAD from first septal perforator to first diagonal and distal LAD defined as distal to first Diagonal branch of LAD. Severity of lesion classified as less than 50%,50-70% and >70% for mild, moderate and severe disease respectively. Severe lesion is characterized into Type A, B and C according to standard definitions. The

data was fed on computer package SPSS (Statistical Packages of Social Sciences) version 11.0. Clinical characteristics were summarized in terms of frequencies and percentages for categorical variables, mean ± S.D. for numerical variables. Test of proportion was used for comparison of categorical variables in diabetics and non diabetics. In all statistical analysis only p-value <0.05 were considered significant.

RESULTS

A total of 150 patients taken, among whom 75 patients (50%) were type-2 diabetics, and 75 (50%) patients were non-diabetic patients. Among diabetic 53 (70.7%) were male and 22 (29.3%) female, while in non-diabetic group 59 (78.7%) were male and 16 (21.3%) female ($p > 0.260$). The age range of patients was 30 to 75 years and the mean age was 51.5 ± 9.5 for diabetics, while 49.4 ± 10.9 for non-diabetics, $p > 0.179$. The mean body mass index in diabetic group was 27.7 ± 4.4 while in non-diabetic group 28.0 ± 6.0 ($p = 0.0722$). Frequency of risk factors for developing coronary artery disease are shown in table 1.

Regarding coronary artery disease in RCA and its severity and location it was found that normal RCA was significantly higher in non diabetics as compared to diabetics. In diabetics there were significantly higher frequency of distal and severe disease. The proximal and mid RCA disease was non significant between two groups (Table 2).

When the severity of disease in left main stem compared between the two groups, it was found that normal LMS was significantly more common in non diabetics but severity of disease was not different between two groups (Table 3).

Location and severity of CAD in left anterior descending coronary artery when compared between the two groups, it was found that normal LAD was more common in non diabetics where as moderate and severe disease was significantly higher in non diabetics. Mild disease was not different statistically in LAD. Regarding location of disease it was found that distal disease was significantly higher in diabetics than non diabetics (Table 4).

The results for location and severity of coronary artery disease in the left circumflex coronary artery in diabetic and non-diabetic patients were also similar. There were more normal circumflex in non diabetics and there were significantly higher proximal and distal disease in diabetics. Mild disease was similar between two groups but moderate and severe disease was more common in diabetics (Table 5).

The results for the extent of coronary artery disease in diabetic as compared to non-diabetic patients were also studied. The prevalence of single vessel disease was more high in non-diabetic patients as compared to diabetic patients, which was statistically highly significant, while the prevalence of three vessels disease was higher in diabetic group as compared to non-diabetic group ($p=0.001$), which is statistically highly significant (Table 6).

There were more type-A lesions in non-diabetic group as compared to diabetic group. The prevalence of type-B lesions was higher in diabetic cohort than non-diabetic group, and the prevalence of type-C lesions was higher in diabetic group as compared to non-diabetic group. This shows that the diabetic group was having more diffuse coronary artery disease as compared to non-diabetic group (Table 7).

DISCUSSION

Diabetic patients have more severe and extensive coronary

Table 1: Risk Factors Distributions in Diabetics and Non-Diabetics

Risk Factors	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Smoker	19	25.3	39	52.0	0.001*
Hypertensive	20	26.7	42	56.0	0.001*
Dyslipidemia	8	10.7	13	17.3	0.239
F/H of IHD	11	14.7	17	22.7	0.208

Table 2: Severity and Location of Coronary Disease in RCA

Location	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Proximal	29	38.7	18	24.0	0.053
Mid	16	21.3	14	18.7	0.683
Distal	35	46.7	13	17.3	0.001*
Severity					
No disease	6	8.0	35	46.7	0.001*
Mild disease	7	9.3	0	0.0	-
Moderate disease	16	21.3	13	17.3	0.535
Significant disease	46	61.3	27	36.0	0.002*

Table 3: Severity of Coronary Disease in Left Main Coronary Artery

Severity	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
No disease	67	89.3	71	94.7	0.028
Mild disease	1	1.3	0	0.0	-
Moderate disease	3	4.0	0	0.0	-
Significant disease	4	5.3	4	5.3	-

Table 4: Severity and Location of Coronary Disease in LAD

Location	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Proximal	29	38.7	28	37.3	0.866
Mid	16	21.3	26	34.7	0.069*
Distal	35	46.7	10	13.3	0.001*
Severity					
No disease	7	9.3	20	26.7	0.006*
Mild disease	3	4.0	3	4.0	-
Moderate disease	39	52.0	27	36.0	0.048
Significant disease	41	54.7	33	44.0	0.0191*

artery disease as compared to non-diabetic patients with ischemic heart disease. The coronary artery disease is more diffuse in diabetic patients that involve long segments of coronary tree and also multiple vessels. So these patients are not ideal candidates for PCI as compared to those which have single vessel disease and more discrete lesions.

In our population the prevalence of diabetes is increasing progressively and so there will be more patients of diabetes and patients of ischemic heart disease. So these patients may be needed early intervention when develop ischemic heart disease and before intervention proper evaluation of coronary anatomy and assessment of severity and extent of disease is mandatory. There are very few angiographic studies even in the world on severity and extent of coronary artery disease specifically in type-2 diabetic and non-diabetic patients suffering of ischemic heart disease. Our study is the first large study in National Institute of Cardiovascular Disease in which we have compared specifically adult type-2 diabetic with non-diabetic patients with ischemic heart disease for assessment of severity and extent of coronary artery disease.

Table 5: Severity and Location of Coronary Disease in LCX

Location	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Proximal	30	40.0	13	17.3	0.002*
Distal	43	57.3	23	30.7	0.001*
Severity					
No disease	11		41	54.7	0.001*
Mild disease	1	1.3	0	0.0	-
Moderate disease	24	32.0	8	10.7	0.001*
Significant disease	45	60.0	27	36.0	0.003*

Table 6: Extent of Coronary Artery Disease Between Diabetic and Non Diabetics

No. of Vessels diseased	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Single vessel disease	4	5.3	35	46.7	0.001*
Two vessel disease	23	30.7	18	24.0	0.359
Three vessel disease	41	54.7	16	21.3	0.001*

This study is important because our urban population has a very high prevalence of ischemic heart disease as compared to rest of the world.[8] The angiographic studies done so far on the diabetic and non-diabetic patients for the assessment of severity and extent of coronary disease most of them show more severe and extensive disease in diabetic as compared to non-diabetic patients with ischemic heart disease.

Natali et al, studied 2253 patients in which 269 patients were diabetic. The mean age 60 ± 7.0, 61 ± 8.0 in the two groups with body mass index (BMI 28.0 ± 4.0, 27.0 ± 3.0). Non diabetic were more hypertensive and smoker than diabetics. There was more prevalence of three vessel disease in diabetic as compared to non-diabetic, 30.5% Vs. 15.1%, p <0.00001 respectively. The CAD was more severe in Diabetic group irrespective of other cardiovascular risk factors like hypertension and smoking. The prevalence of two vessel disease was not statistically significant between the two groups, 26.0 Vs. 21.3.[12] These findings are very close to our study as we found that hypertension and smoking was more common in non diabetics and in our study three vessel disease was more common in diabetics than non diabetics. Our findings of having similar prevalence of double vessel disease in both groups are also supported by Netali et al. The diabetic group consisted of less number of hypertensive and smoker but still diabetics had more severe and extensive disease so this shows the diabetes itself is the main factor for this pattern of disease irrespective of other risk factors. So our results are matching with the results found by Natali et al.[12]

Calton R et al, studied type-2 diabetic and non-diabetic patients angiographically for severity and extent of coronary artery disease. There were total 150 patients, 75 diabetic

Table 7: Comparision of Types of Lesions

Type of Lesion	Diabetics (n=75)		Non-diabetics (n=75)		P-value
	No.	%	No.	%	
Type-A	66	28.8	91	67.9	0.001*
Type-B	88	38.4	23	17.2	0.001*
Type-C	75	32.7	20	14.9	0.001*
Total	229		134		

and 75 non-diabetic with mean age 56.9 ± 7.4 Vs. 56.1 ± 7.7 years. Severity and diffuseness of coronary artery disease was assessed by a coronary artery score (CAS) using the segmental distribution method for coronary artery lesions. Diabetic patients with CAD had a higher CAS (18.7 ± 10.3) as compared to the non-diabetic patients with CAD (12.7 ± 9.6) ($p < 0.01$). Diabetic patients with CAD also had a higher number of three vessel disease as compared to non-diabetic (57.3% Vs. 41.3%, $p < 0.01$).[13] In our study we evaluated the diffuseness of disease in term of type of lesions involving the coronary tree. The lesions involving more than 20mm length of the artery is labeled type C lesion. There was more number of type C lesions in diabetic than non-diabetic patients, (32.7 Vs. 14.9, $p < 0.001$). So diabetics patients were with more diffuse disease as compared to non-diabetic patients. Our result again matching the result found by Calton R et al.[13]

Waldecker B et al, also performed an angiographic study on type-2 diabetic patients for the pattern of CAD. The mean age of patients in this was 66 ± 10 and 61 ± 12. They found more prevalence of multi-vessel disease in diabetic group as compared to non-diabetic group, which strongly supports our finding.[14]

There are also autopsy studies to assess the severity and extent of CAD in type-2 diabetics and non-diabetics. Massori M et al done an autopsy study on 13 diabetic and 22 non-diabetic patients age 60 ± 8.7 and 55.8 ± 10.3, BMI 27.1 ± 3.0 Vs 26.7 ± 3.6. There was more diffuse disease in diabetic than non-diabetic group.[15] Vigorita VJ et al, also performed an autopsy study in which compared 185 diabetic patients with 185 non-diabetic patients with matched age and sex. The diabetic patients have more overall coronary artery disease ($p < 0.002$), more diffuseness of coronary artery disease ($p < 0.005$), more multivessel disease ($p < 0.001$) and more myocardial infarcts, so more left dysfunction ($p < 0.001$).[16] Our study results again matching both these autopsy studies and so favoring that diabetic patients have more severe, diffuse and multivessel disease as compare to non-diabetic patients.

A local study was done in 1990 at National Institute of Cardiovascular disease Karachi on 60 patients, 30 type-2 diabetics and 30 non-diabetic patients with CAD. The SVD was more frequent in non-diabetic group than diabetic group 36.66% Vs. 16.66%, $p < 0.05$, while three vessel disease was more frequent in diabetic group than non-diabetic group, 46.665 Vs. 30%, $p < 0.1$. The diabetic patients were also with more severe disease than non-diabetic group, in which the mean coronary score per patient for diabetics was 11.1 ± 6.36 while for non-diabetic was 8.4 ± 5.96, $p < 0.01$. As compare to this study our study results are matching when compared for three vessel disease and severity of disease. In this study there was no difference statistically between the two groups when compared for distal coronary artery disease 8 Vs. 12.5%, while in contrast to this study in our study there was statistically significant difference between the two groups when was compared for distal disease. This differences may be due to the fact that there was small simple volume, total 60, 30 diabetic and 30 non-diabetics, while our study simple volume was 150, 75 diabetic and 75 non-diabetics. That study was done in 1990, during which the prevalence of diabetes mellitus and CAD-was not so much high as compared to the present prevalence of diabetes and CAD in Pakistani population.[8]

LIMITATIONS

The limitations of coronary angiography are well recognized, starting from the very obvious – viewing 3-dimentional vascular structure in only two dimensions. Also, a visual evaluation of coronary angiograms is hampered by intra- and inter observer variability in analysis. Factors related to vascular remodeling also hinder use of this technique. In a response to preserve lumen dimensions, atherosclerotic vessels have a tendency to dilate. The external diameter of the vessel increases in order to normalize the lumen. Measuring only lumen dimensions thus sometimes offers only a poor estimate of plaque volume in diffuse disease. Furthermore, use of any remodeled vessels diameter as a reference diameter for another stenotic segment may lead to biased results. This may mean that diabetic patients may receive a CABG or PTCA and other types of percutaneous coronary interventions less often than do non-diabetic CAD patients. These treatment methods are applied to treat symptoms of CAD and in some patients populations are shown to improve prognosis and prevent early deaths. Though outcome after these interventions is worse in diabetic than in non-diabetic patients, such interventions are extremely important for diabetic patients who are at high risk for adverse outcome or even death after an acute coronary event such as unstable angina and myocardial infarction, even when treated with thrombolytic agents.[12-14]

More precise knowledge of the severity and extent of CAD in different subtypes of diabetes may reduce the threshold for invasive examinations and improve possibilities for early detection of CAD.

CONCLUSION

It is concluded that coronary artery disease is more aggressive in diabetic patients usually involving more vessels, diffuse in nature, more severe and more complicated in form of type of lesion.

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