Clinical and Angiographic Findings in Diabetic Versus Non-Diabetic Iraqi Patients with Ischemic Heart Disease (A Single Center Experience)

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ABSTRACT:

BACKGROUND:
Diabetes mellitus (DM) is a common, chronic and complex metabolic disorder. Its direct and indirect effects on the vascular system are major causes of morbidity and mortality.

OBJECTIVE:
To verify the effects of diabetes mellitus on clinical presentation and angiographic findings in diabetic patients with ischemic heart disease as compared to non diabetic patients.

PATIENTS AND METHODS:
This cross-sectional descriptive study was conducted in the Iraqi Center of Heart Diseases during the period from November 2008 till June 2009. Two-hundred patients with ischemic heart disease (IHD) who were referred to the Iraqi Center for Heart Diseases were randomly included. Clinical history and examination were done; blood tests, electrocardiography and echocardiography were done for all patients. Patients were classified into 2 groups: 68 patients with diabetes mellitus and 132 patients without diabetes mellitus. Coronary angiography was done for all patients and the results were interpreted by two independent interventional cardiologists.

RESULTS :
There were 145 (72.5 %) males and 55 (27.5 %) females. The mean age of study population was 56.92 ± 3.9 years (56.57 ± 3.2 years for males, 57.91 ± 4.1 years for females).There were no statistically significant differences between diabetic and diabetic patients regarding sex, age, type of clinical presentation, presence of hypertension and family history of coronary heart disease. Diabetic patients were more likely to be smoker (61.7% vs. 48.4%, P = 0.01), to have dyslipidemia (53% vs. 35%, P = 0.03), left ventricular systolic dysfunction (61.7% vs. 48.4%, P = 0.045) left ventricular diastolic dysfunction (92.6% vs. 58.3%, P =0.03), more diseased coronary arteries (38.2% vs. 25.7%, P =0.009), more frequent left main stem involvement (13.2% vs. 3.8%, P =0.008) and more complex coronary lesions (60.2% vs 31.8%, P =0.00002).

CONCLUSION:
Diabetic mellitus has clear adverse effects on left ventricular systolic and diastolic functions and angiographic findings in patients with ischemic heart disease.

KEYWORDS: diabetes, ischemic heart disease, angiography.

INTRODUCTION:

Diabetes mellitus (DM) is a common, complex, and chronic metabolic disease characterized by hyperglycemia with associated disturbances in carbohydrate, fat, and protein metabolism. There are approximately 171 million people worldwide with diabetes, which is expected to increase to 366 million by 2030 because of increased obesity and sedentary lifestyles in both adults and children [1].

The direct and indirect effects on the human vascular tree are the major sources of morbidity and mortality in both type-1 and type-2 diabetes. Generally, the long-term complications of hyperglycemia are separated into macrovascular and microvascular complications. The central pathological mechanism in macrovascular disease is the process of atherosclerosis, which leads to narrowing of arterial walls throughout the body. Atherosclerosis is thought to result from chronic inflammation and injury to the arterial wall in the peripheral or coronary vascular system [2].

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More recent studies have shown that the risk of myocardial infarction (MI) in people with diabetes mellitus is equivalent to the risk in non diabetic patients with a history of previous MI. These discoveries have led to new recommendations by the American Diabetic Association (ADA) and American Heart Association (AHA) that diabetes be considered a coronary artery disease risk equivalent rather than a risk factor [3]. Type 2 diabetes typically occurs in the setting of the metabolic syndrome, which also includes abdominal obesity, hypertension, hyperlipidemia, and increased coagulability. These other factors can also act to promote cardiovascular diseases. Even in this setting of multiple risk factors, type 2 diabetes acts as an independent risk factor for the development of ischemic heart disease, stroke, and death. The presence of microvascular disease is also a predictor of coronary heart events [4]. Patients with type 1 diabetes also bear a disproportionate burden of coronary heart disease. Studies have shown that these patients have a higher mortality from ischemic heart disease at all ages compared to the general population. Atherosclerosis of the coronary, cerebral, and peripheral arteries accounts for approximately 80 % of mortality and 75 % of hospitalizations in persons with diabetes. Following a first cardiac event in people with diabetes, the chance of a second event increases dramatically to 45% [2].

Diabetes is associated with the presence of multiple vulnerable coronary plaques in patients undergoing catheterization for acute coronary syndrome, which may account for the increased risk of re-infarction in these patients. Platelets harvested from patients with diabetes exhibit enhanced aggregation and increased expression of activation-dependent adhesion molecules, such as glycoprotein IIb/IIIa, which contribute to thrombus formation [5]. Patients with diabetes have increased levels of plasminogen activator inhibitor type 1 (PAI-1) in plasma and in atheromas which could decrease fibrinolysis, increase thrombus formation, and accelerate plaque formation [6]. Other vascular changes, including increased endothelin activity and reduced prostacyclin and nitric oxide activity leading to abnormal control of blood flow [7].

No-reflow following successful percutaneous re-canalization of an infarct-related coronary artery occurs more commonly in the presence of diabetes and/or hyperglycemia and may contribute to left ventricular dysfunction [6]. Other diabetes–specific changes that occur include diabetic cardiomyopathy, which impairs myocardial performance and renders the myocardium more susceptible to and less able to recover from ischemia, and diabetic autonomic neuropathy, which results in sympatho-vagal imbalance and contributes to cardiovascular mortality [8]. Patients with diabetes are two-five times more likely to develop heart failure than those without diabetes and following development of heart failure, diabetic patients have higher mortality and heart failure-related morbidity [9]. Due to presumed autonomic neuropathy, asymptomatic coronary heart disease (CHD) can present in several clinical forms including transient episodes of painless myocardial ischemia, silent MI, sudden cardiac death, arrhythmias and ischemic cardiomyopathy [8].

The aim of this study was to study the effects of diabetes mellitus on clinical presentation and coronary angiographic findings in patients with IHD.

PATIENTS AND METHODS:

This study is a cross-sectional descriptive study. It was conducted in the Iraqi Center of Heart Diseases during the period from November 2008 till June 2009. It included 200 patients admitted to the Iraqi Center for Heart Diseases with the diagnosis of ischemic heart disease (chronic stable angina, non ST elevation myocardial infarction/unstable angina or ST elevation myocardial infarction).

Detailed history was taken including age, risk factors for cardiovascular diseases (hypertension, smoking, diabetes mellitus, dyslipidemia and family history of ischemic heart disease) and the cause of referral was ascertained from the medical records of the referring hospital or doctor.

Patients already diagnosed as having diabetes mellitus were considered ((diabetes mellitus)) patients. In patients with diabetes mellitus (DM), questions about onset of the disease, type of treatment, degree of glycemic control were asked. Risk factors were considered according to the informations provided by the patients and/or investigations. Dyslipidemia was defined as increased serum total cholestrol and / or decreased serum HDL cholestrol.

The patients were grouped into 2 groups: 68(34 %) patients with DM and 132 (66 %) patients without DM.

For all patients, electrocardiography (ECG) and troponin test was done to define the type of clinical presentation of ischemic heart disease [Chronic stable angina (CSA), unstable angina/non ST elevation myocardial infarction (UA/NSTEMI), ST elevation myocardial infarction (STEMI)].

Echocardiography was done for all patients for evaluation of left ventricular systolic and diastolic functions was done. Left ventricular systolic dysfunction (LVSD) was defined as left ventricular ejection fraction (LVEF) less than 50 % [10]. Left

ventricular diastolic dysfunction (LVDD) was said to be present if mitral flow E/A ratio is less than 1 and either increased mitral E wave deceleration time (more than 240 msec) or increased isovolumic relaxation time (more than 100 msec) or if evidence of restrictive physiology (E/A ratio more than 2.5 and decreased E wave deceleration time and isovolumic relaxation time) was present [10].

Coronary angiography was then done; angiographic data were reviewed by two interventional cardiologists at the Iraqi Center for Heart Diseases. The extent and severity of coronary artery disease was determined by the number of vessels involved and percentage of diameter stenosis. Significant lesions were said to be present if stenosis of left main stem (LMS) was more than 50% or stenosis of other vessels was more than 70% [11]. The patients were classified into those with single-vessel disease (SVD), two-vessel disease (2VD), three-vessel disease (TVD) and left main stem disease (LMSD). Lesions were also classified according to type of lesions according to the American Heart Association (AHA)/American College of Cardiology (ACC) lesion classification system [11].

Statistical Analysis:
Data were translated into codes using a specially designed coding sheet, and then converted into a computerized database structure. Statistical analyses were done using SPSS (Statistical Package for Social Sciences). The statistical significance of differences in patient groups was assessed by Chi-square test.

Pearson linear correlation coefficient was used to assess the strength and direction of linear correlation between 2 continuous variables. P value less than 0.05 was considered statistically significant.

RESULTS:
Two hundred patients with IHD were included randomly in our study. One hundred and forty-five patients (72.5%) were males and 55 (27.5 %) were females. The age range was 26–87 years and the mean age was 56.92 ± 3.9 years (56.57 ± 3.2 years for males and 57.91 ± 4.1 years for females).

Sixty–eight patients (34%) were diabetics and 132 (66%) were non diabetics. Of patients with DM, 65 patients (98.5%) had type-2 DM and 3 patients (1.5 %) had type-1 DM.

There were no statistically significant differences in the gender distribution and mean age between diabetic and non diabetic groups (table 1). Regarding the presence of other cardiovascular risk factors, there were no statistically significant differences between the two groups for the presence of hypertension and family history of coronary heart disease, while smoking and dyslipidemia were significantly associated with DM (table 1). Regarding the clinical presentation, the study patients were classified into 3 groups (CSA, NSTEMI/UA, STEMI). There were no statistically significant differences between diabetic and non diabetic groups according to different clinical presentations (table 1). Echocardiography was used to assess left ventricular systolic and diastolic functions. Both diastolic and systolic dysfunctions were significantly associated with diabetes mellitus (table 1).

Coronary angiography was done for all patients and classification was done according to number of diseased vessels and type of lesions. Diabetic patients were more likely to have involvement of more vessels and involvement of left main stem than non diabetic ones (table 2). Regarding the type of lesion, patients with DM were more likely to have more complex lesions (type B2 and C) than non diabetic patients (table 2).

Table 1:Comparison between diabetic and non-diabetic patients with ischemic heart disease according to the sex, presence of other cardiovascular risk factors, clinical presentation and left ventricular function.

Parameter	Diabetic patients 68	Non-diabetic Patients 132	Total 200	P value
Sex: Male Female	44(64.7%) 24(35.2%)	101(76.5%) 31(23.4%)	145(72.5%) 55(27.5%)	0.76
Mean age (yr)	57.75 ± 3.1	56.09 ± 4.2	56.92	0.41
Risk factors: Hypertension Smoking Dyslipidemia Family History of CHD	17 (25%) 42 (61.7%) 36(53%) 29(43%)	53 (40%) 64 (48.4%) 36(35%) 63(48%)	70 (35%) 106 (53%) 72(36%) 92(46%)	0.07 0.01 0.03 0.06
Clinical presentation: STEMI NSTEMI/UA CSA	10(14.7%) 18(26.5%) 39(57.35%)	18(13.6%) 39(29.5%) 75(56.8%)	28(14%) 57(28.5%) 114(57%)	0.32 0.49 0.43
Diastolic dysfunction	63(92.6%)	77(58.3%)	140(70%)	0.03
Systolic dysfunction	42(61.7%)	64(48.4%)	106(53%)	0.045

Table 2:Comparison between diabetic and non-diabetic patients with ischemic heart disease according to the number of diseased coronary vessels and type of lesions.

Parameter	Diabetic Patients 68	Non-diabetic Patients 132	Total 200	P value
Number of diseased vessels: Single-vessel disease Two-vessels disease Three-vessels disease	13(19.1%) 20(29.4%) 26(38.2%)	49(37.1%) 44(33.3%) 34(25.7%)	62(31%) 64(32%) 60(30%)	0.009
Left main stem disease	9(13.2%)	5(3.8%)	14(7%)	0.008
Type of lesion*: A B1 B2 C	2(2.9%) 10(14.7%) 15(22%) 41(60.2%)	22(16.6%) 48(36.4%) 20(15.2%) 42(31.8%)	24(12%) 58(17.5%) 35(17.5%) 83(41.5%)	0.00002

* According to the AHA/ACC lesion classification system.

DISCUSSION:

Diabetes mellitus is a common metabolic disorder thataffects a large number of populations all over the world and affects almost all age groups. The effects of DM on macro- and microvasculature are well recognized and affect almost all body organs. The presence of diabetes mellitus in patients with coronary atherosclerotic disease is a marker of poor prognosis, representing a challenge to clinicians, interventional cardiologists, and cardiac surgeons[12].

The metabolic and endothelial changes present in diabetic patients and the higher chance of rupture of the plaque, thrombus formation, and exacerbation of the intimal hyperplasia are determinant factors of a higher incidence of complications and re-stenosis in these patients when they undergo percutaneous coronary interventions. In addition, diabetic patients have more severe angiographic and clinical profiles and usually have associated diseases, such as hypertension, dyslipidemia, coagulopathies, and nephropathies [2].

In the present study, there was no statistically significant difference in gender distribution in diabetic versus non diabetic group. In both groups, males were more commonly affected than females (p value 0.76) (table1).

In a study done by Ane Cecilie Dale et al, it was shown that among people without diabetes, men had twice the rate of IHD compared with women, while in diabetics, the rate of IHD in men and women was identical [13]. Another study conducted by Meithem Hammodi et al demonstrated that diabetic men were predominantly affected by CAD compared with diabetic women [14]. Another study by Keith D. Dawkins et al showed that the percentage of females was more in the diabetic than in the non diabetic cohorts and the difference was statistically significant [15].

Although younger-aged women with diabetes (i.e, <45 years) have an equally low prevalence of atherosclerosis, several studies have reported a significantly higher cardiovascular mortality for women with diabetes compared with men with diabetes. Notably, the age-adjusted prevalence of cardiovascular disease is nearly twofold higher in women with diabetes than in those without diabetes. This may occur because diabetic women lack the premenapousal protection from CAD that is present in non diabetic women [16]. The increased prevalence of IHD in diabetic males compared to diabetic females in the present study may be explained by the

small number of diabetic patients which might not be representative of diabetic population.

In the present study, the mean age of diabetic group was not significantly different from non diabetic group (p value 0.41) (table1). Similar result was found by Keith D. Dawkins et al[15]. This finding should be interpreted cautiously, because diabetes is associated with older age, and this, in turn, with higher prevalence of CHD, especially in women. Andrei Efimov et al showed that the mean age of diabetic patients was significantly more than non diabetic patients [16]. Lopez-Jimenez F et al showed that, compared with non diabetics, patients with diabetes were more likely to be ≤ 60 years old [17].

In this study, smoking and dyslipidemia were more likely to be present in diabetics than in non diabetics (p values 0.01 and 0.03 respectively). On the other hand, there were no statistically significant differences between diabetics and non diabetics for the presence of hypertension and family history of CHD (p values 0.07 and 0.06 respectively) (table 1). Lopez-Jimenez F et al found that, compared with patients without diabetes, patients with diabetes were more likely to have a history of hypertension (70% versus 35%) or high blood cholesterol (35% versus 19%) [17]. José Marconi Almeida de Sousa et al showed that diabetic patients had lower prevalence of tobacco use compared with non diabetics, and no difference was found for the presence of hypertension, family history and dyslipidemia [18].

In the present study, there was no significant difference in clinical presentation of IHD in diabetic versus non diabetic patients (p values for STEMI, UA/NSTEMI and CSA were 0.32, 0.49 and 0.43 respectively) (table 1). JAVIDI Daryoosh et al showed that diabetic patients presented more with myocardial infarction (STEMI or NSTEMI) in comparison with non diabetic patients[19]. Andrei Efimov et al showed that the clinical presentation of IHD in diabetic patients was mainly unstable angina or acute MI[16], while Wadomivo Carlos Manfoi et al showed the prevalence of chronic angina in comparison to acute MI as the main clinical presentation [20]. Keith D. Dawkins et al showed similar prevalence of unstable angina in diabetics and non diabetics and that coronary artery disease in diabetic patients presents less frequently as stable angina [15]. D. Psirropoulos et al showed that the prevalence of acute MI (STEMI) in diabetic patients was similar to that in non diabetic patients [21]. The prevalence of clinical presentation in this study may

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not be representative of the true prevalence of each clinical presentation because the study was conducted in a tertiary center where all patients were referred solely for intervention rather than in a primary or secondary care center where almost all patients firstly present, and this may explain the difference in prevalence of different clinical presentations between this study and other studies.

In this study, diabetic patients were more likely to have LV systolic and diastolic dysfunctions as compared to non diabetic patients (p values 0.045 and 0.03 respectively) (table 1). Sandeep R. Das. et al showed that patients with IHD and diabetes had an increased risk of progression to systolic and diastolic dysfunction compared with IHD patients without diabetes [22]. Similarly, D. Psirropoulos et al showed that systolic dysfunction was greater in diabetic patients, especially in women and that diabetes mellitus had a clear significant negative effect on the systolic function of the left ventricle in the hypertensive patients and supposed that in hypertensive patients with heart failure, the endothelial dysfunction and/or the insufficient treatment of diabetes might contribute to appearance of systolic dysfunction of the left ventricle [21].

Several studies have demonstrated evidence for pre-clinical left ventricular (LV) diastolic dysfunction in patients with diabetes mellitus (DM) independent of coronary disease or hypertension. Several factors are implicated in this finding, including diabetic cardiomyopathy, besides the coronary heart disease itself with ischemia and silent infarctions, which are more frequent in this population [23].

In this study, diabetic patients were more likely to have three-vessel and left main stem disease and less likely to have single- and two-vessel disease as compared with non diabetic patients (P values 0.009 and 0.008 respectively) (table 2). This result is consistent with that reported by Javidi Daryoosh et al that showed that diabetic patients had a higher incidence of three-vessel coronary disease [19] and Lindvall B. et al that showed that the incidence of severe left main coronary disease was significantly higher in diabetic patients than in non diabetic patients and three-vessel disease was significantly more frequent in diabetic patients [24]. José Marconi Almeida de Sousa et al found that the number of severely involved vessels was higher among diabetic patients. Regarding left main coronary artery disease, no difference was found between the two groups [18]. François Ledru et al showed that the incidence of severe left main coronary disease was significantly

higher in diabetic patients than in non diabetic patients. Severe three-vessel disease was also significantly more frequent in diabetic patients [25].

Coronary artery disease in diabetics is characterized by being diffuse, affecting more often the left main and also the distal coronary tree, and had a more rapid progression as compared with non-diabetic patients. This may occurs because myocardial ischemia in diabetic patients typically occurs without symptoms. As a result, diabetic patients have more incidence of multi-vessel coronary atherosclerosis at time of the diagnosis [24].

In this study, diabetic patients were more likely to have more complex lesions (type B2 and C) and less likely to have less complex lesions (type A and B1) as compared with non diabetic patients (p value 0.00002) (table 2).

Lindvall B et al showed that type C lesions of coronary arteries were more common in diabetic than non diabetic patients [24]. On the other hand, Meithem Hammodi et al showed that the types of coronary lesions were similar in both diabetic and non diabetic groups (14). François Ledru et al angiographic study showed that patients with mild type 2 diabetes had a greater prevalence of stenoses of type A, B1 and B2 coronary lesions and two-fold higher occlusion rate than patients without diabetes [25]. Similar findings were found by Shen Wei-feng et al [26]. José Marconi Almeida de Sousa et al showed that the incidence of intracoronary thrombus was not significantly different between diabetic and non-diabetic patients and that of total occlusion was significantly more frequent in diabetic patients (18).

CONCLUSION:

Diabetic patients with IHD are more likely to have LV systolic and diastolic dysfunctions, more likely to have more diseased coronary arteries and involvement of left main stem and more likely to have more complex coronary lesions.

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