

Evaluating coronary artery disease in type 2 diabetes mellitus and Other Risk Factors by angiographic study

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Summary:

Background: Diabetes mellitus (DM) is a metabolic and vascular illness associated with two to four times coronary artery disease (CAD) events and mortality which correlate well with fasting, postprandial plasma glucose and HbA_{1c} level. Other factors such as aging, gender, smoking, dyslipidaemia and hypertension also play an important role in diabetic micro- and macro-vascular complications. Type 2 DM is reported now to be CAD equivalent.

Patients and Methods: A cross sectional study of 118 patients including 90 males and 28 females being 63 diabetics and 55 non-diabetics over the period from March-November 2007 in Iraqi center for cardiac diseases who were underwent coronary angiographic study.

Results: By angiographic study CAD was present in 92.1% of diabetic versus 89.1% in non diabetic patients. Single, double and triple vessels diseases were found in 15.9%, 22.2%, and 42.9% of diabetics versus 16.4%, 21.8%, 34.5% in non diabetics respectively. DM and dyslipidaemias were proved to be independent risk factors for left circumflex artery (LCX) disease predilection (p value <0.05).

Conclusion: Type 2 DM and female gender were reported to be independent risk factors for LCX and left main stem coronary arteries respectively while age, smoking, and dyslipidaemia were independent risk factors for coronary atherosclerotic. Hypertension and family history were proven to be dependent atherosclerotic risk factors and this may suggest that risk factors for the presence of CAD may differ from those affecting angiographic extent and severity. CAD was more extensive and severe in post menopausal women in this study.

Keywords: Coronary artery disease, Type 2 Diabetes mellitus, risk factors, angiographic study.

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Introduction:

Diabetes mellitus is worldwide metabolic and vascular problem characterized by hyperglycemia with or without micro or macro-vascular complications due to relative deficiency of pancreatic insulin secretion and/ or resistance to its action. Diabetes mellitus is classified according to American diabetes association (ADA) and world health organization (WHO) into type 1 and 2. The diagnosis depends on specific criteria in 2003 as [Fasting blood sugar (FBS) \leq 126 mg/dl, random blood sugar (RBS) \leq 140mg/dl, and oral glucose tolerance test (OGTT) 2hr \geq 200 mg/dl] in the presence of symptoms (polyuria and polydipsia) but those with impaired glucose tolerance test (IGTT) (180-200mg/dl) are considered pre- diabetic (1,2,3,4). Coronary artery disease and mortality are two to fourfold higher in type 2 diabetic patients, being associated with poor glycaemic control, genetic susceptibility, dyslipidaemias and hypertension that augment micro-, macro- vascular complications and the process of atherosclerosis. (5) Diabetic patients are more likely to have multivessel-disease and fewer collateral vessels (6, 7). Pathogenesis of coronary vascular endothelial dysfunction and atherosclerosis in diabetes mellitus is induced by hyperglycemia (Glucose toxicity), inflammatory and immune mediated mechanisms.

Markers such as plasma fibrinogen, C- reactive protein, interleukin 6, plasminogen activator inhibitory factor (PA-I) and other cytokines are detected in these patients (8, 9, 10, 11, 12). Intensive glycaemic and hypertensive control studies (United Kingdom Prospective Diabetes Study UKPDS and Diabetes Control and Complications Trial DCCT) revealed no significant changes in cardiovascular and cerebral complications versus conventional diabetic therapy but it has been suggested that metformin therapy reduced macro-vascular events. (13) Active treatment of coronary ischemia including revascularization is associated with great benefit as evidenced by many medical reports, so findings from pathological and angiographic studies confirming more diffuse and distal atherosclerosis in diabetic patients highlight the value of coronary angiography to define the optimal therapeutic strategy but it is not recommended as a screening test though it will determine the severity of the underlying atherosclerotic lesions especially the presence of left main stem artery (LMS), three vessels-disease, or proximal left anterior descending artery (LAD) disease in patients with moderate or high risk as evidenced clinically and by non invasive cardiologic testing, beside to that it can determine the suitability of the coronary vessels for percutaneous interventions or surgical bypass where indicated, keeping in mind its risks are negligible when compared to under taking therapy with incomplete and in accurate information. (5)

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Patients and methods:

One hundred and eighteen diabetic and non diabetic patients underwent coronary angiographic study for suspected coronary artery diseases (CAD) between 1st of March to 30th of November 2007 in the Iraqi center for cardiac diseases and for each full history was undertaken looking for risk factors like age, smoking, hypertension (HT), DM, gender, family history and dyslipidaemias. They were investigated primarily by Chest X-ray (CXR), electrocardiography (ECG), Echocardiography, FBS, and lipid profile. The normal or abnormal coronary artery anatomy as decided by the degree of luminal narrowing expressed in percentage of the prestenotic diameter showing normal LAD, left circumflex artery (LCX), ramus and right coronary artery (RCA). The degree of narrowing scale was on follows: 0% narrowing, stenosed (25-50%, 51-70%, 71-90%, 91-99% and 100% as non significant, significant, non clinical critical, subtotal and total obstruction respectively) while LMS considered critical if narrowing was >50%. The clinical variables were set accordingly as three age groups (<45, 46-59 and 60 year or more), male or female gender, being hypertensive, diabetic dyslipideamic, smoker and family history of CAD as evidenced by simple history, use of anti-hypertensive, anti-diabetic medication, or FBS >126 mg/dl, RBS> 200/dl, lipid-profile (low density lipoprotein LDL>100 mg/dl, high density lipoprotein HDL<50 mg/dl in female or <40 mg/dl in male or serum triglyceride TG> 250 mg/dl or both of them), 10 cigarettes/day or more and lastly cardiac events, angioplasty, coronary bypass surgery, sudden death in the 1st degree relatives under age 55 year for men and 65 year in female.

Results:

Table (1): A total number of 118 patients were enrolled in the study with age ranged between 38-84 years. Ninety males (76.3%) and 28 females (23.7%) so male:female ratio was 3:1, positive history of smoking, ex-smoking, diabetes, hypertension dyslipidaemias and family history of CAD were 38(32.2%), 30(25.4%), 63(53.4%), 74(62.7%), 38(32.2%) and 63(53.4%) respectively. Table (2): Showed distribution of studied sample by gender and certain clinical variables including age, DM, family history, HT, dyslipidaemias and smoking but the statistical significant difference between males and females was present only in hypertension and smoking where p value <0.05. Table (3): Showed distribution of diabetic and non diabetic cases according to site and severity of coronary artery involvement, revealing significant statistical difference (p value <0.05) between diabetic and non diabetic left circumflex (Lcx) artery involvement while there was non significant difference in involvement of other coronary arteries. Table (4): showed distribution of diabetic and non diabetic patients according to number of coronary artery involvement and revealing single, double and triple vessels disease (15.9%, 22.2% and 42.9%) in

diabetic versus (16.4%, 21.8% and 34.5%) in non diabetics respectively. Coronary angiographic study showed non statistical significant difference between diabetic and non diabetic regarding the total and number of coronary artery involvement where p value >0.05.

Table (1) Demographic characteristics of studied patients

		No.	%
Age(mean±SD)	58.15	58.15	9.32
Gender	Male	90	76.3
	Female	28	23.7
Smoking	Non smoker	50	42.4
	Smoker	38	32.2
	ex-Smoker	30	25.4
Diabetes mellitus	NO	55	46.6
	Yes	63	53.4
Hypertension	NO	44	37.3
	Yes	74	62.7
Family history of CAD	NO	55	46.6
	Yes	63	53.4
Hyperlipidemia	NO	80	67.8
	Yes	38	32.2

Table (2) the distribution of studied patients by gender and certain variables

		GENDER				P-value
		Male		Female		
		No.	%	No.	%	
AGE	<45 years	8	8.90	2	7.10	0.92
	46-60 years	34	37.80	10	35.70	
	>60 years	48	53.30	16	57.10	
DM	No	44	48.9	11	39.3	0.37
	Yes	46	51.1	17	60.7	
Family history of CAD	No	41	45.6	14	50.0	0.68
	Yes	49	54.4	14	50.0	
Hypertension	No	40	44.4	4	14.3	0.004'
	Yes	50	55.6	24	85.7	
Hyperlipidemia	No	60	66.7	20	71.4	0.63
	Yes	30	33.3	8	28.6	
Smoking	Non smoker	32	35.6	18	64.3	0.026'
	smoker	32	35.6	6	21.4	
	ex-smoker	26	28.9	4	14.3	

Table 3. Distribution of Diabetic and non Diabetic patients according to site and severity of coronary artery involvement:

		Diabetes Mellitus				P-value
		No		Yes		
		No.	%	No.	%	
LAD	Normal	6	10.9	10	15.9	0.13
	<50%	1	1.8	8	12.7	
	51-70%	4	7.3	4	6.3	
	71-90%	23	41.8	26	41.3	
	Subtotal	6	10.9	7	11.1	
	Total	15	27.3	8	12.7	
LCX	Normal	20	36.4	16	25.4	0.03
	<50%	1	1.8	4	6.3	
	51-70%	4	7.3	3	4.8	
	71-90%	22	40.0	28	44.4	
	Subtotal	4	7.3	-	-	
	Total	3	5.5	12	19.0	
RCA	Normal	22	40.0	27	42.9	0.80
	<50%	4	7.3	2	3.2	
	51-70%	2	3.6	4	6.3	
	71-90%	18	32.7	23	36.5	
	Subtotal	3	5.5	3	4.8	
	Total	6	10.9	4	6.3	
RAMUS	Normal	51	92.7	61	96.8	0.31
	71-90%	4	7.3	2	3.2	
LMS	Normal	50	90.9	54	85.7	0.51
	<50%	2	3.6	2	3.2	
	>50%	3	5.4	7	11.1	

Table 4: Distribution of diabetic and non diabetic patients according to number of coronary artery involvement:

No. of coronary arteries	Diabetes Mellitus				Total		P-value
	Non		Yes		No.	%	
	No.	%	No.	%			
Normal	6	10.9	5	7.9	11	7.9	0.84
single	9	16.4	10	15.9	19	9.3	0.62
Two	12	21.8	14	22.2	26	22	0.08
Three	19	34.5	27	42.9	46	39	0.04
Four	9	16.4	7	11.1	16	13.6	0.42
Total	55	100	63	100	118	100	

Discussion:

In this study we found that normal coronary artery anatomy is more common in non-diabetic than in diabetic patients but this difference was statistically not significant (p value >0.05), while single and double vessels disease were more common in diabetic than non diabetic patients but it was not significant statistically. Diabetic patients also showed sever LCX artery stenosis while other coronary arteries are affected equally in both diabetic and non diabetic patients and this is in agreement with pajunen et al study,(14) waller et al,(15) Hochman et al,(16) and Iraqi studies like Abd Al Ameer et al(17) but in disagreement with other studies (18,19) that show that the extent of the disease in the coronary arteries is greater in diabetic patients revealing higher incidence of multi-vessel disease (66% vs 46%). This may be mostly explained by coronary endothelial dysfunction and

atherosclerotic process induced by diabetic (glucose toxicity), inflammatory and immune mediated mechanisms.(11,12) We found that age, gender, smoking, dyslipidaemia and type 2 DM had independent risk effect but their effectiveness differs according to the coronary vessel involved. Dyslipidaemia increases the severity of coronary artery atherosclerotic lesion through LDL injured endothelial and smooth muscle cell proliferation augmenting inflammatory progression and atheroma formation(20) and this in agreement with national and international studies (17)and(21,22) respectively. Smoking had statistically significant positive correlation with coronary artery disease by vascular endothelial damage, enhancing platelet adhesion and atheroma formation.(23) and this is in agreement with national and international studies (17)and(24,25) In this study it was found that coronary artery diseases were more severe and extensive in women than men and this could be explained by the age of women that included in the study which was about 58 years, i.e post menopausal women that they have low HDL as anti-risk factor this was in agreement with national study (26) but in disagreement with national and international studies (17) and (27,28) respectively. In our study CAD are more sever and extensive with aging process as evidenced in national and international studies (26) and (29, 30) respectively and in fact most new onset CAD now occurs after age of 65 years, this trend is highly pronounced in women due to high absolute risk in elderly patients so chance of primary prevention in this age group should be substantial. Hypertension was reported in our study as dependent risk factor for CAD as evidenced also by most epidemiological data and more recent studies showing low CAD, stroke and heart failure by antihypertensive therapy and this was in agreement with national studies (17,26). Positive family history of premature CAD was independent risk factor in other studies (31) and in disagreement with ours possibly because most of the causes of sudden death not underwent postmortem assessment. The lack of significant difference in this study in diabetic and hypertensive patients is possibly related to small size sample and earlier referring of such patient to coronary angiographic study due to high suspicion of CAD for any chest pain that turned to be non cardiac in origin.

Conclusion:

Types 2 DM patients are at higher risk for sever multiple CAD and more in post-menopausal women due to lower HDL anti-risk factor with more predilections for left circumflex artery independently. Family history, hypertension, DM and gender are poor predictive factors for CAD severity. Limitation of study: This study does not correlate the severity of CAD to the degree of glycemic control because of limitation of resources for assessment of HbA_{1c} in our hospital which is vital for assessment of degree of glycemic control.

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