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Prevalence of Silent Coronary Artery Disease Among Patients with Type 2 Diabetes Mellitus in Suleimani, Iraq

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ABSTRACT

Objectives: To study the prevalence of silent coronary artery disease among patients with Type 2 Diabetes Mellitus and associated variables.

Methods: A cross sectional multi-center design study in the Sulaymaniyah city. The data collected from patients admitted to medical wards of Shar teaching Hospital, Shahid Hemn teaching Hospital and Faruq medical city. It was conducted during the period of 10 months starting from April 2017 to Jan 2018. All patients with type 2 Diabetes Mellitus without symptoms of coronary heart disease were included. Symptoms were evaluated by history, physical examination including blood pressure measurement and searching for other risk factors. The patients were investigated for HbA1c, Lipid profile, resting Electrocardiography (ECG), Echocardiography, Exercise Treadmill test, and CT coronary angiography.

Results: A total of 106 patients, 55 male (51.9%) and 51 female (48.1%) were enrolled in this study, the mean age of the patients was (58.50 yr ± 10.94), Nine (8.4%) patients had ischemic change by resting ECG, 10 (9.4%) had ischemic change by Echocardiography, Exercise treadmill test (ETT) was done for 20 patients and revealed positivity for ischemia in only 3 (15%) patients, CT coronary angiography was done for three patients and were conclusive for CAD.

Conclusion: Silent coronary artery disease is common in patients with type 2 diabetes mellitus, therefore patients with DM should be carefully evaluated to detect early cardiovascular adverse effect to avoid fatal consequences.

Keywords: Coronary artery disease, Type 2 Diabetes Mellitus, silent ischemia, electrocardiography

Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by impairment in the metabolism of carbohydrates, lipids and proteins.[1] The number of adults with diabetes worldwide is expected to increase from 135 million in 1995 to more than 300 million by 2025. DM is a major health problem which is tightly linked to development of coronary artery disease (CAD). Majority of CAD burden will be subclinical until it presents without warning as sudden death, myocardial infarction, cardiac failure, or arrhythmia.[2]

Diabetes mellitus has been well depicted as a cardiovascular risk factor in developed countries. In the Framingham study, the incidence of cardiovascular disease among diabetic men was two times that among nondiabetic men, and similarly was three times more increased in diabetic women compared to nondiabetic women.[3]

Risk factors for progression of the cardiovascular disease in patients with diabetes include: obesity, cigarette smoking, systemic hypertension, dyslipidemia, chronic renal disease. Glycemic control lowers the risk of vascular diseases, by reducing the production of advanced glycosylation end-products, the agglomeration of which is thought to promote atherosclerosis.[4]

Patients with type 2 DM have been indicated to have an elevated risk of coronary artery disease (CAD; 1.7-folds in men; 2.5-folds in women), premature death related to CAD and heart failure (2.2-folds in men; 5.4-folds in women).[5]

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium; it typically happens when there is an imbalance between myocardial oxygen supply and demand. The main reason of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional decreasing in myocardial blood flow and insufficient perfusion of the myocardium supplied by the involved coronary artery.[6]

Silent Ischemia

After coronary artery occlusion, left ventricular mechanical abnormalities and electrocardiogram (ECG) abnormalities precede the development of symptoms. Silent ischemia is typically known as objective evidence of myocardial ischemia in patients without symptoms associated with that ischemia. It may be detected in patients who have no symptoms during an exercise or pharmaceutical stress test but who do have transient ST-segment changes, perfusion defects, or reversible regional wall motion abnormalities.[7]

Asymptomatic myocardial ischemia has been displayed to happen more often than symptomatic ischemia in patients with stable CAD. Similarly, nearly one-half of patients admitted with unstable angina will have silent ischemia detected during continuous ECG assessment. 12% of Type 2 DM with no symptoms suggestive of CAD had abnormal exercise ECGs, although only one-half of these patients were found to have perfusion defects during thallium scintigraphy.[8]

In a study, 33% of diabetic patients with at least one additional cardiovascular risk factor had silent ischemia. At the end, even healthy patients without risk factors for CAD have been illustrated to have silent ischemia.[9]

While diabetics and non-diabetics without evidence of CAD are screened for ischemia, there is a higher incidence of silent ischemia in the former, 6.4–22% and 2.5–11%, respectively.[10] Non-specific or atypical symptoms, like dyspnea, epigastric pain, and confusion were reported by 32% to 42% of

diabetic patients with AMI comparison with 6% to 15% of non-diabetic patients.[11]

Patients with diabetes develop CAD at an accelerated rate and have a higher incidence of heart failure, myocardial infarction, and cardiac death than their nondiabetic counterparts.[12]

Mechanism of Silent Myocardial Ischemia

Silent ischemia causes by variable combinations of reduced sensitivity to painful stimuli and coronary microvascular dysfunction.[13] The association between diabetes and both silent ischemia and 'painless infarctions' has been attributed to autonomic neuropathy.[14] Patients with silent ischemia have been shown to have a higher threshold for other forms of pain, such as that resulting from an electric shock, limb ischemia, and cutaneous application of heat or balloon inflation in the coronary artery.[15]

Another area of investigation makes a suggestion that silent ischemia may be because of cerebral cortical dysfunction, rather than peripheral nerve dysfunction. Frontal cortical activation appears to be essential to experience cardiac pain, and some evidence shows that in patients with silent ischemia, afferent pain impulses from the heart are subject to abnormal neural processing.[16] Increased degrees of beta-endorphin, an endogenous opiate, have been noted in patients with asymptomatic myocardial ischemia during exercise.[17]

Association of diabetes autonomic neuropathy with silent ischemia: The afferent fibers running into the cardiac sympathetic nerves form the fundamental pathway for the transmission of cardiac pain. It is reasonable to expect that diabetic autonomic neuropathy interferes with the afferent cardiac sensory impulses in view of the frequent abnormalities faced in efferent parasympathetic and sympathetic cardiac control. The concept that autonomic destruction is responsible for the increased frequency of painless infarctions in the presence of diabetes is based primarily on an early autopsy series in which different levels of neuropathic change in the visceral pericardial nerve fibers of all five diabetic patients with silent myocardial infarction but not in five patients with painful infarctions were found.[18]

Figure 1 describes the suggested testing algorithm for the asymptomatic diabetic patient. Although a resting ECG with abnormalities suggestive of CAD warrants further testing, the utility of ambulatory monitoring of ECG ST-segment changes to detect CAD in general asymptomatic populations has been disappointing and not cost-effective.[10]

Patients and Methods

This cross sectional, prospective study was conducted during the period of 10 months from April, 2017 to Jan, 2018. (106) patients with Type 2 diabetes mellitus in Shar teaching Hospital, Shahid Dr. Hemn Teaching Hospital and Faruq medical city in Sulaimani city were included, 55 patients were male and 51 were female, all of the patients were on anti-diabetic medication, all of them underwent ECG, Echocardiography and 20 patients underwent treadmill test (TMT), CT coronary angiography was done for 3 patients only. A form designed to collect demographic data; name, age, gender, smoking, body mass index, duration of diabetes mellitus, and the results of Random blood glucose, HbA1c, Blood Pressure, Lipid profile, Electrocardiogram, Echocardiography, Exercise ECG, Coronary CT Angiography.

Ethical Consideration

This thesis was approved by scientific and ethical committee of Iraqi Board for Medical Specializations and consent taken from the authorities of Shar teaching Hospital, Shahid Dr. Hemn teaching Hospital and Faruq Medical city in Sulaimani.

Verbal consent was from all patients to enroll to the study, and confidentiality was taken in consideration.

Statistical Analysis

Data of this study were analyzed in bioscience center for scientific and medical research. The data was analyzed using statistical software SPSS version 21. Frequency, and percentages of the data were calculated, numerical variables were expressed as mean ± standard deviation. Chi square was used to find the relation between the categorical variables, the level of significant were considered if *P*-value ≤0.05.

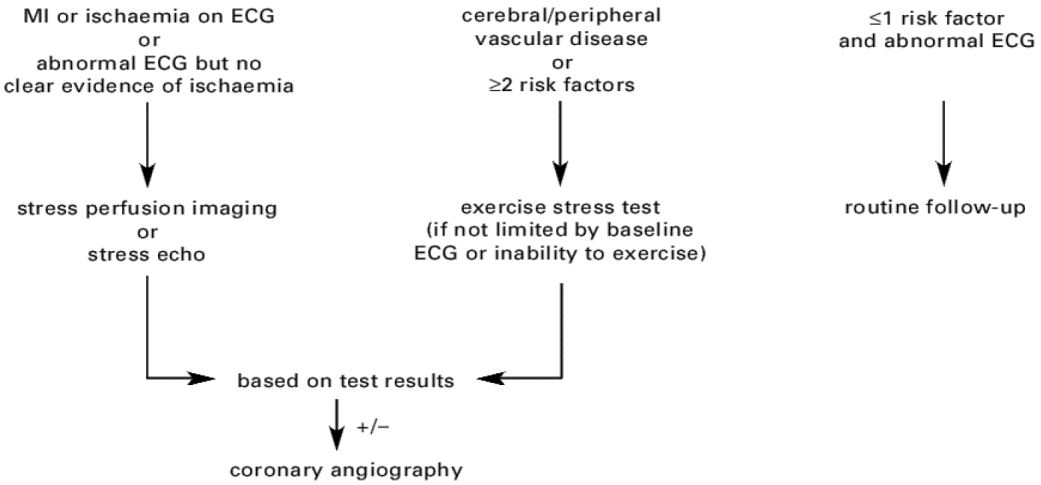

Fig. 1 **Cardiac testing algorithm for the asymptomatic diabetic patient.**[10]

Results

The Mean age of the study population was 58.50 ± 10.94 years, age range (35–85), the Mean BMI (25.09 ± 4.47) kg/m^2, ranging (18–50). The Mean duration of DM was (8.54 ± 5.84) years, ranging (1–27), the Mean RBS was (222.63 ± 77.98) mg/dl ranging (97–500). The Mean HbA1c was (8.44 ± 2.05%) ranging (5.7–17.8), these results are shown in Table 1.

Forty five (42.5%) patients had hypertension, 74 (69.8%) patients had dyslipidemia, 4 (3.8%) patients had family history of IHD, and 13 (12.3%) patients had history of smoking, these results are shown in Table 2.

All patients were on anti-diabetic medication, 11 of them were controlled and 95 of them were not controlled, according to the HbA1c results. Nine (8.4%) patients had ECG finding of ischemic heart disease, the blood sugar was controlled in 1 patient & uncontrolled in 8 patients, of these patients 8 were male, and these results are shown in Table 3.

Echocardiographic findings suggestive of ischemia were present in 10 (9.4%) of the cases, 8 males and 2 females, the blood glucose was controlled in 1 patient & not controlled in 9 patients, Table 4.

Treadmill test was done for 20 patients and was positive in 3 (15%) of them, all were non-control and all were male, these results are shown in Table 5.

CT coronary angiography was done for 3 patients, all were males, the results were positive in all of them and they

Table 1. **Characteristics of the studied patients**

Variables	Mean ± SD	Minimum	Maximum
Age (years)	58.50 ± 10.94	35	85
BMI (kg/m^2)	25.09 ± 4.47	18	50
DM duration (years)	8.54 ± 5.84	1	27
RBS (mg/dl)	222.63 ± 77.98	97	500
HbA1c %	8.44 ± 2.05	5.7	17.8

Table 2. **Risk factors of coronary heart disease other than diabetes mellitus**

Risk factors		Frequency	Percentage
Hypertension	Yes	45	42.5
	No	61	57.5
Dyslipidemia	Yes	74	69.8
	No	32	30.2
Smoker	Yes	13	12.3
	No	93	87.7
Family history of IHD	Yes	4	3.8
	No	102	96.2

Table 3. **ECG abnormality among controlled and non-controlled diabetes mellitus according to HbA1c & Gender**

	ECG		Total	*P*-value
	Normal No. (%)	Abnormal No. (%)		
HbA1c%				
Control (≤6.5)	10 (10.3)	1 (11.1)	11 (10.4)	
Non-control (≥6.5)	87 (89.7)	8 (88.9)	95 (89.6)	
Total	97 (100.0)	9 (100.0)	106 (100.0)	**0.967**
Gender				
Male	47 (48.5)	8 (88.9)	55 (51.9)	
Female	50 (51.5)	1 (11.1)	51 (48.1)	
Total	97 (100.0)	9 (100.0)	106 (100.0)	**0.020**

≠ *P*-value was calculated using Fisher Exact Test.

Table 4. **Ischemic change by Echocardiography among controlled and non-controlled diabetes mellitus with HbA1c & Gender**

	Echocardiography		Total	*P*-value
	Normal No. (%)	Abnormal No. (%)		
HbA1c				
Control	10 (10.4)	1 (10.0)	11 (10.4)	
Non-control	86 (89.6)	9 (90.0)	95 (89.6)	
Total	96 (100.0)	10 (100.0)	106 (100.0)	**0.967**
Gender				
Male	47 (49.0)	8 (80.0)	55 (51.9)	
Female	49 (51.0)	2 (20.0)	51 (48.1)	
Total	96 (100.0)	10 (100.0)	106 (100.0)	**0.062**

Table 5. **Treadmill results among controlled and non-controlled DM with HbA1c & Gender**

	Treadmill		Total	*P*-value
	Normal No. (%)	Abnormal No. (%)		
HbA1c				
Control	3 (17.6)	0 (00.0)	3 (15.0)	
Non-control	14 (82.4)	3 (100.0)	17 (85.0)	
Total	17 (100.0)	3 (100.0)	20 (100.0)	**0.430**
Gender				
Male	8 (47.1)	3 (100.0)	11 (55.0)	
Female	9 (52.9)	0 (0.0)	9 (45.0)	
Total	17 (100.0)	3 (100.0)	20 (100.0)	**0.089**

underwent Percutaneous Coronary Intervention, the blood glucose was controlled in one patient & not controlled in 2 patients.

Discussion

The diagnosis of CAD generally is missed or delayed in diabetic patients because the typical symptoms of cardiac ischemia are often masked. As a result, multi-vessel atherosclerosis often is present before ischemic symptoms occur and before treatment can be instituted.[19]

In this study, treadmill test was positive in 3 patients among 20,(15%). Other studies like Milan Study on Atherosclerosis and Diabetes (MiSAD) Group,[20] Fornengo et al.,[21] S. Sejil et al.,[22] and Ditchburn et al.,[23] showed variable results (12.1% , 17.1% , 24% and 36%) respectively.

The positive treadmill test was mostly among uncontrolled diabetic patient 3 patients who had uncontrolled diabetes, but statistically not significant because of fewer numbers of cases included, this result is consistent with that of DeLuca et al.[24] in which incidence of silent ischemia increases with poor blood glucose control.

The positive treadmill test was more common in male than female, in this study all positive cases were male, same as Fornengo et al.[21] The Exercise Treadmill Test was positive in 19 of 111 patients (17.1%); five were female (26.3%) and 14 were male (73.7%), and Janand-Delenne et al.,[25] 24 of 130 patients (18.4%), including eighteen men and 6 women.

Most of the patients in this study who had positive results for silent myocardial ischemia by ECG, Echocardiography, Exercise treadmill test, CT coronary angiography were more than 60 years old, (60%) mean age were (63.6) years old similar to Inoguchi et al.[26] which showed that elderly NIDDM patients (aged over 60 years) may have an extremely high prevalence of silent myocardial ischemia (26.3%).

Most of the patients that were positive for silent myocardial ischemia by ECG, Echocardiography, Treadmill Test, CT coronary angiography had at least one other risk factor than DM for coronary artery disease, three (30%) of positive patients had only diabetes mellitus and 9 (69%) had also other risk factors (from 2–4 risk factors) similar to the results of DeLuca et al.[24] which showed that silent myocardial ischemia increased as the number of risk factor increased, 20 patients had 5 risk factors for CAD, 9 (45%) patients were positive, 365 had 3 to 4 risk factors for CAD, 90 (25%) patients were positive, 451 had 0 to 2 risk factors for CAD, 87 (13%) patients were positive.

Conclusion

Silent coronary artery disease is common in patients with type 2 diabetes mellitus, especially in the presence of other risk factors & in those over 60 years of age, therefore diabetic patients must be carefully evaluated to avoid fatal consequences.

Conflict of Interest

None.

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