

Silent Ischaemia in Patients with Type 2 Diabetes mellitus

Ghulam Hussain Balouch, Samiullah Shaikh, Syed Zulfiqar Ali Shah,
Bikha Ram Devrajani, Nadia Rajpar, Neelam Shaikh and Tarachand Devrajani

Department of Medicine, Liaquat University of Medical and Health Sciences Jamshoro, Sindh, Pakistan

Abstract: This study was carried out to determine the frequency of silent ischaemia in patients with Type 2 Diabetes mellitus at Liaquat University Hospital Hyderabad. This comparative study was conducted in department of Medicine, Liaquat University Hospital Hyderabad. All the diabetic patients from the diabetic clinic were registered for study and 100 non diabetic patients were selected for control. Both diabetic and control group patients were assessed for silent ischemia by exercise tolerance test (ETT) on treadmill. Result revealed that during 6 month period a total of 376 was registered for study. Of these 193 were male and 183 were female 298 their mean age was 48.4 ± 7.2 . Of these 185 were diabetic and 191 were non diabetic, 56 were smoker and 320 non smoker, hypertension was present in 262 and 114 were normotense, family history of IHD present in 171 whereas 205 patient have no family history. The exercise tolerance test was positive in 37% diabetic patients whereas it is positive in 22% non diabetic patients. In conclusion, the diabetic patients are more prone to acquire silent myocardial ischemic changes and the frequency is increased with additional identified preexisting risk factor.

Key words: Ischemia • Diabetes mellitus • Type 2 diabetes

INTRODUCTION

Diabetes is associated with increasing cardio metabolic disorders. Micro and macro vascular complication of diabetes are responsible for mortality and morbidity in these patients [1]. The risk of macro vascular complication more than micro vascular complications [1]. Coronary artery disease is found in diabetics four times higher than normal subjects and cause mortality is 80% of type 2 diabetes patients [2, 3]. In most diabetic patients diagnosis of coronary artery disease is delayed because of canceled symptoms [4, 5]. Falcone *et al.* [6] found 8 to 26% prevalence of CAD in asymptomatic type 2 diabetes patients. Chipkin *et al.* [7] reported that prevalence of asymptomatic ischaemia diagnose ETT was not significantly different in diabetic and non diabetic patients (54% and 47% respectively). Other study Nesto *et al.* [8] compared 50 patient non diabetic patient only 28% of diabetic patients experience angina during treadmill test compared with 68% of non diabetic. Patient with diabetes have a higher incidence of triple vessels coronary artery disease and may also diffuse disease coronary artery disease in non diabetic patients [9, 10]. We plan to performed such study locally by assessing the frequency

of silent ischemia in diabetic patients at Liaquat University Hospital, Hyderabad. The present study shall help us making guidelines for investigating and planning management of such patients.

MATERIAL AND METHOD

This comparative study of six months was conducted at Liaquat University Hospital Hyderabad, a tertiary care teaching hospital. All the diabetic patients from the diabetic clinic were registered for study and 100 non diabetic patients were selected for control. Diabetic patient were evaluated for presence of risk factors i.e. family history of ischemic heart diseases, high blood pressure, smoking, dyslipidemia. Both diabetic and control group patients were assessed for silent ischemia by exercise tolerance test on treadmill. The informed consent was taken from every patient for participation in the study and all the maneuvers were under the medical ethics. The inclusion criteria of the study were diabetic and non diabetic (for control), age 30 to 70 years, either gender, the resting ECG within normal limits, while the exclusion criteria were patients with Ischaemic changes in resting ECG, patients with previous history of Angina,

MI, patients have LBBB, RBBB in resting ECG, unable to perform exercise, orthopedic problems, patient above 70 years, diabetic patients with asthma, COPD, patient with heart failure and renal failure. Regarding ethical justification all the expenses of the study were paid with the cooperation of whole research team. The data was collected on pre-designed proforma and was entered, saved and analyzed in SPSS version 10. The frequency and percentage will be calculated for silent ischemia in diabetic patients. The frequency and percentage will also be calculated for gender distribution. The mean and SD will be calculated for numerical variables. The chi-square test was applied at 95% confidence interval and the p-value ≤ 0.05 will be considered as statistically significant.

RESULTS

During 6month period, a total of 376 was registered for study. Of these 193 were male and 183 were female p.o298 their mean age was 48.4 + 7.2.Of these 185 were diabetic and 191 were non diabetic. 56 were smoker and 320 non smoker, hypertension was present in 262 and 114 were normotense, family history of IHD present in 171 whereas 205 patient have no family history. The mean±SD of different parameters of the study were shown in table1. There is significant difference [p = 0.04] in age distribution between diabetic and non diabetic (Table 2). ETT was positive in 111 of 376 patients statically significant (p=<0.01) difference was observed in diabetic then non diabetic (Table 3). In male diabetic ETT was significantly positive [P=0.003] then non diabetic, whereas no significant difference was observed diabetic and non diabetic female patients.

Table 1: Mean and Standard Deviation of Different Parameters

Parameter	Mean±Std. Deviation
Age (in years)	48.85±7.50
Systolic blood pressure (mmHg)	132.94±13.76
Diastolic blood pressure (mmHg)	86.10±6.60
HbA1c	7.924±1.342
Duration	8.87±3.642
Cholesterol (mg/dL)	204.78±40.59

Table 2: Age Distribution In Diabetic and Non Diabetic Population

Age	Diabetes Mellitus			P-value
	Yes	No	Total	
≤ 40	14	27	41	0,04*
> 40	171	164	335	
Total	185	191	376	

*Statistically significant

Table 3: Exercise Tolerance Test (ETT) In Diabetic and Non Diabetic Subjects

Diabetes mellitus	ETT		Total	P-value
	Negative	Positive		
Yes	116	69	185	0.001*
No	149	42	191	

*Statistically significant

DISCUSSION

Silent ischemia is defined as transient and reversible decrease in oxygen supply to myocardium.it is more frequent in diabetic non diabetic individuals [11]. Premature onset and rapid progress of arteriosclerosis occurs in type2 diabetes. This is due to loss of normal endothelial function. In type 2 diabetic early endothelial damage occurs concomitantly with hyperglycemia hypertension, dyslipidemia and hyperinsulinemia [12]. Patients suffering from type2diabtes more then 10 year were recommended for routine stress test [13]. A study found frequency of silent ischemia of 42.5% in type2 diabetics whose has duration of diabetes more then 10 years [14]. Male gender is risk of atherosclerosis. In this study 40 out of 100 diabetic male has ETT positive.These results were also observed in the study on atherosclerosis and diabetes. Silent ischemia of 12.4 found in Turkish study [13] which demonstrates that there is no significant difference in the severity of coronary disease or in the prevalence of silent ischemia between male and female patients. However, among the patients identified by exercise ECG females have higher body mass index than males, suggesting that obesity may represent the risk factor of CAD in women with type 2 diabetes [14]. On the other hand the study of Hussein *et al.* [15] reported the prevalence of SMI in asymptomatic microalbuminuric and normalbuminuric type 2 diabetic patients was 30 and 6.6% respectively. Current guidelines recommended screening of silent ischemia in selected high cardiovascular patients whose has age above 60 years and two or more cardiovascular risk factors [16].

In addition, some [17, 18] but not all clinical studies support the hypothesis that SMI is more frequent in diabetic patients as compared with non diabetic individuals. A higher risk of death is signi?cantly associated with ST segment depression during the test, irrespective of the presence or absence of angina. Finally, among patients with SMI, mortality rate is higher in diabetic than in non-diabetic subjects and, in the former group, survival rates are improved by revascularization in

respect to pharmacological treatment. Taken together, these data suggest a strong indication that those patients with T2D having additional risk factors for CAD should be screened for SMI [19]. A local study conducted on 100 diabetic individual at Khyber Teaching Hospital, Peshawar shown 44 (44%) had SMI, of 44 patients with SMI, 25 (57%) were male and 19 (43%) were female and their Mean age was 57.00 ± 2.79 [20].

The exercise stress test is a provocative test which in diabetic patients may have a higher positive predictive value for SMI than other non-invasive tests, including ECG, 24-hr ambulatory ECG monitoring and thallium tomographic imaging [20]. However, up to date, no information on the applicability and diagnostic accuracy of this test has been available in asymptomatic patients with T2D. The lack of information on accuracy is due to the fact that in previous studies [21, 22] coronary angiography was not performed in patients negative at the screening test.

Therefore, the present study had shown the applicability and accuracy of exercise tolerance test for screening for SMI in asymptomatic T2D patients with additional risk factors for CAD. The results obtained in terms of accuracy clearly indicate that the ETT may be proposed as the first test for screening for SMI in the population.

In conclusion, diabetic patients are more prone to acquire silent myocardial ischemic changes and the frequency is increased with additional identified preexisting risk factor. Further studies are needed in various hospitals to evaluate the diabetic patients as far as ischemic changes are concerned and also to investigate which other non-invasive test may be chosen and to validate it in order to eventually propose a rationale and applicable flow chart for screening for SMI in high-risk diabetic patients.

REFERENCES

1. Cade WT., 2008. Diabetes-Related Microvascular and Macrovascular Diseases in the Physical Therapy Setting. *Phys. Ther.*, 88(11): 1322-35.
2. Nazimek-Siewniak, B., D. Moczulski and W. Grzeszczak, 2002. Risk of macrovascular and microvascular complications in Type 2 diabetes: results of longitudinal study design. *J. Diabetes Complications*, 16(4): 271-6.
3. Lincoff, A.M., 2003. Important Triad in Cardiovascular Medicine: Diabetes, Coronary Intervention and Platelet Glycoprotein IIb/IIIa Receptor Blockade. *Circulation.*, 107: 1556.
4. Flaherty, J.D. and C.J. Davidson, 2005. Diabetes and coronary revascularization. *JAMA*, 293(12): 1501-8.
5. Bowden, D.W., A.B. Lehtinen, J.T. Ziegler, M.E. Rudock, J. Xu, L.E. Wagenknecht, D.M. Herrington, S.S. Rich, B.I. Freedman, J.J. Carr and C.D. Langefeld, 2008. Genetic epidemiology of subclinical cardiovascular disease in the diabetes heart study. *Ann Hum. Genet.*, 72(5): 598-610.
6. Falcone, C., L. Nespoli, D. Geroldi, C. Gazzaruso, M.P. Buzzi, C. Auguadro, L. Tavazzi and P.J. Schwartz, 2003. Silent myocardial ischemia in diabetic and nondiabetic patients with coronary artery disease. *Int J. Cardiol.*, 90(2-3): 219-27.
7. Chipkin, S.R., D. Frid, J.S. Alpert, S.P. Baker, J.E. Dalen and N. Aronin, 1987. Frequency of painless myocardial ischemia during exercise tolerance testing in patients with and without diabetes mellitus. *Am. J. Cardiol.*, 59(1): 61-5.
8. Nesto, R.W., R.T. Phillips, K.G. Kett, T. Hill, P. Edward, E. Young and O.S. Leland, 1988. Angina and Exertional Myocardial Ischaemia in diabetic and non diabetic patients: assessment by exercise thallium scintigraphy. *Ann. Intern Med.*, 108: 170-75.
9. Waller, B., P. Palumbo and W. Robert, 1980. Status of Coronary arteries at necropsy in Diabetes Melitus with onset after age 30 years. *AM. J. Med.*, 69: 498 -506.
10. Barold, G., G. Falzi and F. Mariani, 1979. Sudden Coronary death post mortum study in 208 selected cases compared to 97 control subjects. *Am. Heart J.*, 98: 20-31.
11. Caracciolo, E.A., B.R. Chaitman, S.A. Forman, P.H. Stone, M.G. Bourassa, G. Sopko G.N.L. Geller and C.R. Conti, 1996. Diabetics with coronary disease have a prevalence of asymptomatic ischemia during exercise treadmill testing and ambulatory ischemia monitoring similar to that of nondiabetic patients. An ACIP database study. ACIP Investigators. Asymptomatic Cardiac Ischemia Pilot Investigators. *Circulation*, 15-93(12): 2097-105.
12. Kharlip, J., R. Naglieri, B.D. Mitchell, K.A. Ryan and T.W. Donner, 2006. Screening for silent coronary heart disease in type 2 diabetes: clinical application of American Diabetes Association guidelines. *Diabetes Care*, 29(3): 692-4.
13. William, S.B., J.A. Cusco, M.A. Rody, M.T. Johnstone and M.A. Creager, 1996. Impaired nitric oxide mediated vasodilatation in patients with non insulin dependent diabetes mellitus. *J. Am. Coll. Cardiol.*, 27: 567-574.

14. Levine, E., L. Young, H. Siu, A. Srivastava, J. Davey and F.J.T. Wackers, 2009. Silent CAD and 5-year outcome in asymptomatic patients with type 2 diabetes with abnormal ECG in the DIAD study. *J. Nucl. Med.*, 50(Supplement 2): 1.
15. Hussein, A.Z.F. and S.K. Strak, 2006. Silent Myocardial Ischemia and Microalbuminuria in Asymptomatic Type-2 Diabetic Patients. *Pak J. Med. Sci.*, 22(2): 116-21.
16. Stern, S. and S. Sclarowsky, 2009. The ECG in Diabetes Mellitus. *Circulation.*, 120: 1633-1636.
17. Naka, M., K. Hiramatsu, T. Aizawa, A. Momose, K. Yoshizawa, S. Shigematsu, F. Ishihara, A. Niwa and T. Yamada, 1992. Silent myocardial ischemia in patients with non-insulin-dependent diabetes mellitus as judged by treadmill exercise testing and coronary angiography. *American Heart J.*, 123: 46-53.
18. Ambepityia, G., P.G. Kopelman, D. Ingram, M. Swash, P.G. Mills and A.D. Timmis, 1990. Exertional myocardial ischemia in diabetes: a quantitative analysis of anginal perceptual threshold and the influence of autonomic function. *J. Am. Coll. Cardiol.*, 15(1): 72-7.
19. Bacci, S., M. Villella, A. Villella, T. Langialonga, M. Grilli, A. Rauseo, S. Mastroianno, S. De Cosmo, R. Fanelli and V. Trischitta, 2002. Screening for silent myocardial ischaemia in type 2 diabetic patients with additional atherogenic risk factors: applicability and accuracy of the exercise stress test. *Eur. J. Endocrinol.*, 47(5): 649-54.
20. Ahluwalia, G., P. Jain, S.K. Chugh, H.S. Wasir and U. Kaul, 1995. Silent myocardial ischaemia in diabetics with normal autonomic function. *International J. Cardiol.*, 48: 147-153.
21. Koistinen, M.J., 1990. Prevalence of asymptomatic myocardial ischaemia in diabetic subjects. *British Medical J.*, 301: 92-95.
22. Inoguchi, T., T. Yamashita, F. Umeda, H. Mihara, O. Nakagaki, K. Takada, T. Kawano, H. Murao, T. Doi and H. Nawata, 2000. High incidence of silent myocardial ischemia in elderly patients with non insulin-dependent diabetes mellitus. *Diabetes Res. Clin. Pract.*, 47(1): 37-44.