

**Original Article**

Early recognition of Ischemic Heart Disease (IHD) in asymptomatic type 2 diabetes mellitus patients in malwa region

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Abstract

Background: Type II Diabetes Mellitus (DM) is a key risk factor for ischemic heart disease (IHD). Patients remain generally asymptomatic and thus diagnosed at an advance stage of the illness. Our aim of study was to identify the IHD at an early stage in asymptomatic diabetic patients.

Methods: 136 patients of type 2 Diabetes who remains asymptomatic were enrolled prospectively for treadmill test (TMT) followed by coronary angiography (CAG), which was performed on 96 (70.87%) TMT positive patients. Status of diabetes, clinical features including risk factors, TMT and angiographic findings were examined.

Results: The patients were divided into two groups, high risk group A (risk factor ≥ 2) and low risk group B (risk factor ≥ 1). 34 patients of group A (36.95%) were IHD positive out of 92 patients of high risk group and 4 patients group B (9.09%) out of 44 patients of low risk group. Period of diabetes mellitus and multiple risk factors were correlated with ischemic heart disease (IHD) as well as multiple coronary artery involvement.

Conclusions: A regular TMT for all asymptomatic type 2 diabetic cases (≥ 10 years) with family history of IHD and subsequent CAG should be done in all cases who tested positive for TMT, for early recognition of IHD to take suitable revascularization methods.

Keywords: Type 2 diabetes mellitus, Risk factor, TMT, CAG, Early detection of IHD, Revascularization.

Introduction

Type 2 diabetes mellitus is a significant risk factor for ischemic heart disease (IHD). The Framingham Heart study discovered increase incidence from one to five fold of IHD, MI, CHF, PAD and sudden death in type 2 diabetes mellitus patients.¹ IHD accounts for 70-80% of mortalities in DM.⁵ The lack of chest pain is common (silent ischemia) in type 2

DM patients. It is not easy to diagnose the disease at proper time as of asymptomatic nature of the disease progression.^{2,7} The prognosis of person with type 2 diabetes who have ischemic heart disease is poorer than non-diabetic due to association of multiple vessels.^{1,5,6}

American Diabetes Association (ADA) recommends that treadmill exercise test (TMT) and/or coronary angiography should be done in

diabetic patients having additional cardiovascular risk factors.² More sensitive investigative tools such as Single Photon Emission Computerized Tomography (SPECT) and multi-detector coronary MDCT may be done. But those diagnostic approaches cannot be done for asymptomatic patients on an out patients basis.⁷ No commonly established test suggested for early diagnosis of asymptomatic IHD.

Nevertheless severe IHD may be diagnosed noninvasively by TMT with fewer cardiac risk factors on out patients basis.⁷ In the present study TMT was done in asymptomatic type 2 DM patients regardless of cardiac risk factors and CAG in positive TMT cases for early recognition of IHD.

Methods

This study was done from January 2018 to July 2018 at Shri Aurobindo medical college and PG Institute in the department of medicine amongst the type 2 DM patients who came for routine checkup in the OPD. Exclusion criteria 1) Typical history of angina 2) Know non coronary heart disease such as congenital or acquired valvular heart disease, heart failure (CCF) or arrhythmia 3) Abnormal ECG finding 4) Diagnosed IHD by invasive and non-invasive procedure.

Clinical feature, blood biochemistry and 5 cardiac risk factors, such as hypertension, dyslipidemia, family history of IHD, smoking habit and macro-micro albuminuria were noted. Patients were placed in 2 groups group A with risk factor ≥ 2 and group B with risk factor ≥ 1 .

Type 2 DM were defined as 1) Random blood sugar level ≥ 200 mg/dl and diabetic symptoms based on ADA diagnostic criteria 2) Fasting blood sugar level ≥ 126 mg/dl. 3) Diagnosed and receiving treatment for DM. Duration of type 2 DM is taken a time period between diagnosis of DM to IHD evaluation in years. Diabetic retinopathy, neuropathy and nephropathy were evaluated with appropriate clinical and laboratory testing. Lipid profile was done in every patients.

TMT was performed in all patients irrespective of number of cardiac risk factors. Coronary angiography (CAG) was performed in positive,

inconclusive and equivocal TMT result. This study was approved by hospital ethical committee and informal consent was taken from all TMT positive patients.

Treadmill exercise test (TMT) was performed according to Bruce protocol. TMT was defined as +ve if there was ≥ 1 mm horizontal/down sloping ST-segment for 0.08 sec. after the J point. Coronary angiography was performed in all TMT +ve, inconclusive and equivocal cases. Coronary artery disease was considered if there was more than 60% stenosis. In case of $>80\%$ stenosis then appropriate Percutaneous Coronary Intervention (PCI) and CABG were done.

Statistical analysis

The data obtained were input into the SPSS statistical software, version 20.0. A descriptive statistical analysis was performed. P value was set significant at <0.05 .

Results

There were 136 asymptomatic type 2 diabetic patients male (n-65), female (n-20). The clinical characteristics are shown in Table 1. The Mean BMI was 24.8 of which more than 50% of the patients were overweight. Mean duration of DM was 10.1 years. Most of the patients were dyslipidemic. The average IHD risk factors were two.

Table 1: CVD risk factors, clinical characteristics & diabetic complications evaluation of the studied patients

	Total No. of patients (N-136)	IHD		P value
		Yes (N-38)	No (N-98)	
Age (years)	56.2 ± 6.4	58 ± 6	54.6 ± 6.5	0.004
Male/female	116/20	34/4	82/16	0.5899
DM duration years	10.44 ± 6.4	12.8 ± 6	8.4 ± 6.4	0.0002
F/H/O DM	52 (38.2%)	22 (57.8%)	30 (30.6%)	0.0055
Retinopathy	22 (16.1%)	10 (26.3%)	12 (12.2%)	0.0818
Neuropathy	30 (22.0%)	10 (26.3%)	20 (20.4%)	0.0672
Hypertension	60 (44.11%)	28 (73.6%)	32 (32.6%)	0.0001
F/H/O IHD	20 (14.7%)	16 (42.1%)	4 (4.8%)	0.00001
Smoking	80 (58.8%)	30 (78.9%)	50 (51.0%)	0.0034
No. risk factor	2.0 ± 1	3 ± 1	2 ± 1	0.0001
HBA _{1c} %	8 ± 2	8 ± 1	9 ± 1	<0.0001
Creatinine (mg/dl)	1.1 ± 0.8	1.3 ± 0.6	1 ± 0.4	<0.0009
Total cholesterol (mg/dl)	196 ± 40.2	210 ± 38	196 ± 41	0.0706
HDL (mg/dl)	40 ± 10	42 ± 6	44 ± 9	0.2085
LDL (mg/dl)	126 ± 32	122 ± 36	114 ± 38	0.2657
Ttglyceride (mg/dl)	206 ± 132	202 ± 119	226 ± 120	0.2961

We compared CVD risk factors between patients with IHD & patients without IHD (Table 1). Those with IHD were older, smoker, hypertensive, positive family history of IHD, long duration of diabetes, high HBA_{1C}, high serum creatinine level & more number of CVD risk factors. No significant differences were found in gender, diabetic complications, total cholesterol, HDL/LDL cholesterol & triglyceride level

Table 2: comparison of risk factor and IHD findings

	Group A (risk factors ≥ 2)	Group B (risk factors ≥ 1)	P value
	N-92	N-44	
Age (years)	56.4 \pm 8.6	55.4 \pm 8.1	0.519
Male/female	80/12	38/6	0.924
BMI (kg/m ²)	26 \pm 2.6	25.8 \pm 4.8	0.753
F/H type 2 DM	30 (32%)	14 (31%)	0.926
Duration of type 2 DM	10.4 \pm 6.5	8.9 \pm 6.8	0.217
Retinopathy	25 (27%)	8 (18%)	0.3521
Neuropathy	20 (21%)	10 (22%)	0.066
HBA _{1C} %	8.2 \pm 2.2	7.6 \pm 2.0	0.1281
Incidence of IHD	34 (36.95%)	4 (9.09%)	0.0015
Multivessel disease	20 (66%)	5 (62%)	0.2207

Analysis of risk factors

The total enrolled 136 patients were divided into two groups (Table 2). High risk group Gr-A (risk factors ≥ 2) and low risk group (Group B) (risk factors ≥ 1). 92 patients (76.64%) had ≥ 2 risk factors (Group A) and 44 patients (32.36%) had ≥ 1 risk factor (Group B). No significant difference in age, gender, BMI, family history of DM, duration of DM, HBA_{1C} level & complications of diabetes were found between group A & group B (Table 2). The prevalence of IHD in group A and group B was 36.95% and 9.09% respectively. These data correlates the risk factors with IHD incidence. The more the risk factors, the more chance of IHD incidence. The multi vessel involvement in group A was 66% & group B 62% and didn't differ much between the two groups. Thus we can conclude that even asymptomatic diabetic patients with fewer risk factors may have multi vessel involvement.

Discussion

Diabetes is a major risk factor of Ischemic heart disease as revealed by Framingham study. There is

marked increase in PAD, CHF, IHD and SCD (risk increased from one to five fold).¹ AHA has designated DM as a "IHD risk equivalent" type 2 DM patients without prior MI have a similar risk for IHD related events as non-diabetic individuals who had a prior MI. Prognosis of individuals with diabetes who have IHD or MI is worse than for non-diabetic.² IHD is more likely involve multiple vessels in individuals with DM due to silent nature of IHD in type 2 DM. Mostly the patients are diagnosed at the advance stage of disease with multiple organ failure and leads to high mortality rate.⁸⁻¹¹

The mortality and morbidity of type 2 DM are mostly due to cardiovascular disease. The common pathophysiology of IHD in DM is due to endothelial dysfunction. The vascular tone, leukocyte attraction, vascular smooth muscle growth, nutrient delivery and end product nutrient removal, inflammation, coagulation, thrombosis and fibrinolysis are regulated by vascular endothelium. The alteration of vasoconstriction, inflammation thrombosis and fibrinolysis collectively causes endothelial dysfunction and along with vascular smooth muscle and platelets dysfunction cause the micro and macro vascular complication of type 2 DM. Type 2 DM leads to dyslipidemia in the form of hypertriglyceridemia, reduced HDL and increase LDL level which is more atherogenic and more easily glycated and susceptible to oxidation. This dyslipidemia with hyperinsulinemia enhance initiation and growth of atherosclerotic coronary plaques formation. Diabetic patients commonly show higher incidence of cardiac ischemia than non-diabetic patients. Silent Ischemia may delay or mask the diagnosis of IHD. When IHD is diagnosed it is most advanced and multi vessel diseases. Autonomic neuropathy which damage the afferent sympathetic fibers may be the causative pathophysiology along with dysfunction of opioid receptors damage to the nerve ending may be the cause silent ischemia in type 2 DM.¹⁷⁻¹⁹

ADA recommended specific guideline for search of risk factors in asymptomatic diabetic patients.² The approach is based on CVD risk factor such as smoking, dyslipidemia, hypertension, family story

of IHD and micro-macro albuminuria. Those risk factors are well known CVD risk factors.^{12,16} Our study corroborates with those risk factors for IHD. Our patients were truly asymptomatic and enrolled from the out patients department. ADA did not include duration of DM among IHD risk factors. Several studies concluded a positive relation of duration of DM with IHD.^{12,14,15} Our study also revealed positive correlation of duration of DM with IHD incidence.

Diagnostic approach of IHD may fail if consideration strict to number of risk factors only. Our study revealed and suggests an active IHD evaluation in relatively older patients with duration of type 2 DM $> \pm 10$ years and positive family history of IHD. It is advisable to consider the duration of DM as a primary risk factor regardless of symptoms. To overcome the delay of diagnosis of IHD more sensitive diagnostic techniques are evolved such MDCT and SPECT.^{3,7} These modern tools are more promising with higher accuracy but they are costly and can only be done at referral hospital. TMT is less costly and can be done for screening IHD in asymptomatic type 2 DM patients in on outpatient basis.

Conclusions

TMT & subsequent CAG in TMT positive patient is the right approach considering the cost benefit ratio of all asymptomatic relatively older diabetic patients with ≥ 10 years of duration and positive family history of IHD with even fewer CVD risk factors for early detection of IHD and necessary revascularization before multi vessel involvement and multiple organ failure.

Our study results are limited as the sample size is small. Larger sample size & using more modern diagnostic techniques may corroborate our findings.

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Ethical approval: The study was approved by the hospital ethics committee

References

1. Kannel WB, McGee DL. Diabetes and glucose tolerance as risk factors for cardiovascular disease: the Framingham study. *Diabetes Care*. 1979;2:120-6.
2. American Diabetes Association. Consensus development conference on the diagnosis of coronary heart disease in people with diabetes. *Diabetes Care*. 1998;21:1551-9.
3. Lim S, Choi SH, Choi EK, Chang SA, Ku YH, Chun EJ, et al. Comprehensive evaluation of coronary arteries by multidetector-row cardiac computed tomography according to the glucose level of asymptomatic individuals. *Atherosclerosis*. 2009 Jul;205(1):156-62.
4. Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA guideline for exercise testing: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 1997;30:260-311.
5. Bonow Ro, Bohannon N, Hazzard W. Risk stratification in coronary artery disease and special populations. *Am J Med*. 1996;101:4A17S-22S.
6. Haffner SM, Lehto S, Ronnema T, Pyorala L, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetics subjects with and without prior myocardial infarction. *N Engl J Med*. 1998;339:229-34.
7. Wachkers FJ, Chyun DA, Young LH, Heller GV, Iskandrian AE, Davey JA, et al. Resolution of asymptomatic myocardial ischemia in patients with type 2 diabetes in the detection of ischemia in asymptomatic diabetics (DIAD) study. *Diabetes Care*. 2007;30:2892-8.
8. Brun E, Nelson RG, Bennett PH, Imperatore G, Zoppini G, Verlato G, et al. Diabetes duration and cause specific mortality in the Verona Diabetes Study. *Diabetes Care*. 2000;23:1119-23.
9. Stamler J, Vaccaro O, Neaton JD,

- Wentworth D. Diabetes, other risk factors, and 12-years cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care*. 1993;16:434-44.
10. Chiariello M, Indolfi C. Silent myocardial ischemia in patients with diabetes mellitus. *Circulation*. 1996;93:2089-91.
 11. Haffner SM. Coronary heart disease in patients with diabetes. *N Engl J Med*. 2000;342:1040-2.
 12. Janand-Delenne B, Savin B, Habib G, Bory M, Vague P, Lassmannvague V. Silent myocardial ischemia in patients with diabetes: who to screen. *Diabetes Care*. 1999;22:1396-400.
 13. Koistinen MJ. Prevalence of asymptomatic myocardial ischemia in diabetic subjects. *BMJ*. 1990;301:92-5.
 14. Milan study on Atherosclerosis and Diabetes Group. Prevalence of unrecognized silent myocardial ischemia and its association with atherosclerotic risk factors in noninsulin-dependent diabetes mellitus. *Am J Cardiol*. 1997;79:134-9.
 15. Langer A, Freeman MR, Josse RG, Steiner G, Armstrong PW. Detection of silent myocardial ischemia in diabetes mellitus. *Am J Cardiol*. 1991;67:1073-8.
 16. Foster MC, Hwang SJ, Larson MG, Parikh NI, Meigs JB, Vasani RS, et al. Cross-classification of microalbuminuria and reduced glomerular filtration rate: associations between cardiovascular disease risk factors and clinical outcomes. *Arch Intern Med*. 2007;167:1386-92.
 17. Chan JC, Malik V, Jia W, Kadowaki T, Yajnik CS, Yoon KH, et al. Diabetes in Asia: epidemiology, risk factors, and pathophysiology. *JAMA*. 2009;301:2129-40.
 18. D'Agostino RB Sr, Vasani RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: Framingham Heart study. *Circulation*. 2008;117:743.
 19. Libby P, Ridker PM, Hansson GK, Leducq Transatlantic Network on Atherothrombosis. Information in atherosclerosis: from pathology to practice. *J Am Coll Cardiol*. 2009;54:2129-38.