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Correlation of Microalbuminuria with Ischemic Heart Disease in Type II Diabetics

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Abstract: ***Type 2 Diabetes is a common and serious disease leading to chronic, mostly irreversible macro and microvascular complications. Coronary Artery Disease is the leading cause of death in patients with Type II Diabetes Mellitus and is very often asymptomatic and silent. It may present without warning as Acute Myocardial Infarction, Heart Failure, Arrhythmia or sudden death, thus emphasizing the potential value of identifying high-risk individuals with diabetes who are having Silent Myocardial Ischemia. Microalbuminura is now considered as a cardiac risk marker and can easily measured in the lab. The present study was undertaken to assess the correlation of microalbuminuria with silent Myocardial Ischemia in patients of Type 2 DM.The results of the study showed that 64 % of asymptomatic patients with microalbuminuria had a positive treadmill exercise test. Hence we can deduce from this study that microalbuminuria is an independent risk factor for silent myocardial ischemia. Screening Type 2 Diabetes patients for microalbuminuria can identify a subset of patients who should be screened early for Silent myocardial Ischemia, so as to save high mortality and morbidity associated with silent myocardial infarction.***

1. Introduction

*The prevalence of diabetes mellitus is increasing worldwide. It is estimated that globally 382 million people live with diabetes and the International Diabetes Federation expects this number to rise to 592 million by 2035.*Diabetes leads to chronic, mostly irreversible macro and microvascular complications. Coronary Artery Disease is the leading cause of death in patients with Type II Diabetes Mellitus is often asymptomatic [(1)] and silent and may present without warning as Acute Myocardial Infarction, Heart Failure, Arrhythmia or sudden death. Silent Myocardial Ischemia is of particular concern in diabetic patients. It is suspected that partial or complete autonomic denervation in diabetic causes impaired symptom perception e.g. lack of recognition of chest pain leading to Silent Myocardial Ischemia. [(2)]

Two forms of Silent Myocardial Ischemia are recognized. The first and less common form, designated Type-I Silent Ischemia, occurs in patients with obstructive Coronary Artery Disease (CAD), who do not experience angina at any time. The second and much more frequent form, designated Type -II Silent Ischemia, occurs in patients with the usual forms of chronic stable angina, unstable angina, and Prinzmetal's angina. These patients exhibit some episodes of ischemia associated with chest discomfort and others without pain. [(3)] Silent myocardial ischemia (SMI) can be detected by using cardiac stress testing. Silent Myocardial Ischemia has been defined as exercise induced ST depression of >1mm in the absence of Coronary Artery Disease symptoms. [(4)]One parameter which can help in assessing the risk of developing silent myocardial Ischemia is microalbuminuria. Microalbuminuria is present in approximately 25% of patients with Type II Diabetes and is associated with a doubling of the risk of early death, mainly from Coronary Heart Disease[(5)]. Microalbuminuria has been defined by consensus, as a urinary albumin excretion rate between 30 and 300 mg/day. [(6)] Persistent microalbuminuria has also been associated with an increased risk of atherosclerosis and cardiovascular mortality. Therefore, patients with diabetes should be screened regularly for microalbuminuria.[(7)]

2. Aims and Objectives

The primary aim of the study was to study the correlation of microalbuminuria with silent myocardial Ischemia (as detected by abnormal exercise stress test) .

3. Methodology

This was prospective observational hospital based study carried out in Mahatma Gandhi Mission Medical College Hospital, Kamothe, Mumbai, a 740 bedded tertiary care teaching hospital for a period of one and a half years. A total of 50 OPD patients were enrolled on the basis of inclusion and exclusion criteria. All patients diagnosed with Type II diabetes as per the ADA guidelines within the age group of 30 years to 65 years, who were asymptomatic and had normal baseline ECG and were voluntarily willing to participate in the study , after voluntary informed consent were included in the study.

Patients with complaints of chest pain or any history of Ischemic heart disease or its treatment, abnormal ECG, history of hypertension, Type 1 DM or any other form

diabetes mellitus eg MODY, LADA etc, thyroid disease, any kidney disease like nephritic or nephrotic syndrome, any acute illness including UTI (which can alter albumin excretion rates), abnormal ECG, any contraindication for Treadmill Stress Test, patients on drugs like Angiotensin converting Enzyme Inhibitors and Angiotensin Receptor blockers and pregnant woman were excluded from the study.

Demographic profile was recorded for each patient. Type 2 Diabetic patients were put into 3 groups according to chronicity of diabetes mellitus Group 1 = DM < 5 years, Group 2 = DM 6-10 years, Group 3 = DM 11 – 15 years. A complete clinical examination was carried out in each patient with particular reference to the screening of complications of diabetes like retinopathy, nephropathy, neuropathy, diabetic foot, and ischemic heart diseases. Fundus was examined in all the patients for diabetic changes and the details were recorded and were classified as Normal, Non Proliferative Diabetic Retinopathy, Proliferative Diabetic Retinopathy. Body mass index (BMI) was calculated. ECG was done for all patients. Only those with normal resting ECG were included in the study. Patients with no history or symptoms of Ischemic Heart Disease and normal resting EEG were screened for microalbuminuria (By Immuno-turbidimetric method). Biochemical Investigations evaluated were Fasting & Post Prandial Blood Sugar, HbA1C, Serum .Creatinine. Each of patients enrolled in the study was subjected to Exercise Stress Test after obtaining proper voluntary consent of stress test.

4. Statistical Analysis

All the above mentioned data was collected and then subsequently analyzed at the end of the study. Statistical analysis was done in consultation with a trained Biostatistician.Methods used were Pearson's chi – square test and appropriate Non – Parametric statistical tests.

5. Results

In the present study, 64 % of asymptomatic patients with microalbuminuria had a positive treadmill exercise test. 73 % males with microalbuminuria had a positive treadmill exercise and 50 % female patients with microalbuminuria had a positive treadmill exercise test. 71 % of patients in the age group of 60 years and above with microalbuminuria had a positive treadmill exercise test. 86 .2% patients with HbA1C >9% had positive treadmill test. In the present study, 70.8 % patients with duration of diabetes in the range 11-15 years had positive treadmill test. 82 % of obese, 45 % of normal and none of the underweight patients had positive treadmill. Hence we observe from this study that microalbuminuria is an independent risk factor for silent myocardial ischemia. Microalbuminuria is also associated with greater predisposition for silent myocardial ischemia in males than in the females. Poor glycemic control is associated with greater predisposition for silent myocardial ischemia. Greater predisposition for silent myocardial ischemia was also observed with increasing age, longer the duration of diabetes and increasing BMI. As seen in other studies this study also showed that the prevalence of microalbuminuria increased with worsening glycemic control, with increasing duration of diabetes, with increase in BMI and in patients of Diabetic Retinopathy.

Table 1: Correlation of Silent Myocardial Ischemia with Microalbuminuria

Stress Test	Number Of Cases	Percentage	Chi Value	P value	Result
Positive	32	64.0	15.34	0.002	Significant
Negative	18	36.0	3.21	0.141	Not significant
Total	50	100			

In the present study, 64 % of diabetic patients with microalbuminuria had a Positive Stress Test.

Table 2: Correlation of Silent Myocardial Ischemia with Glycemic Control

HBA1C	Total Number Of Cases	Number Of Positive Cases	Percentage Of Positive Cases	Chi-Value	P – value	Result
< 7	6	1	16.67	15.972	0.002	Significant
7-9	15	6	40	16.476	0.002	Significant
>9	29	25	86.21	19.752	0.001	Highly Significant
TOTAL	50	32				

25 out of 29 (86 .2%) of diabetic patients (with microalbuminuria) with Hba1c > 9 had Positive Treadmill Test.

Table 3: Correlation of Silent Myocardial Ischemia with Duration of Diabetes

Duration of D.M	Total Number of Cases	Number of Positive Cases	Percentage of Positive Cases	Chi-Value	P – value	Result
< 5	8	2	33	18.763	0.004	Significant
6-10	20	13	65	22.534	0.002	Significant
11-15	24	17	70.8	25.943	0.001	Highly Significant
Total	50	32		15.533	0.004	Significant

17 Out of 24 (70.8 %) of diabetic patients (with microalbuminuria) with history of Diabetes more than 10 years had a Positive Treadmill Test.

6. Discussion

In this study it was observed that 64% of asymptomatic Type 2 DM patients with microalbuminuria had positive stress test, implying Silent myocardial ischemia.

Duration of diabetes may play significant part in microvascular damage by prolonged periods of hyperglycemia induced Advanced Glyaction End products (AGE) accumulation over years. In a study done by Patel et al [(8)], the authors showed that the prevalence of microalbuminuria increased progressively with the duration of diabetes, which was also shown in this study. Microalbuminuria was found in 40 % of patients with

history of Diabetes for 6- 10 years and in 44 % of patients who were diagnosed as having Diabetes for more than 10 yrs.

Ahluvwalia G [9] found that 70% subjects with diabetes for more than 5 years duration had associated silent myocardial ischemia while only 30% subjects with diabetes less than 5 years duration had an associated silent myocardial ischemia. Serginj et al conducted a study [10] including 500 patients with type 2 diabetes mellitus with normal resting ECG and found that, 12.4% patients had asymptomatic coronary artery disease on exercise treadmill testing. The abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$). In the present study 17 out of 24 (70.8 %) patients with history of diabetes more than 10 years had a positive treadmill test .This was statistically significant.

Another significant observation was that 25 out of 29 (86 .2%) patients with Hba1c > 9 had positive treadmill test. This was statistically significant (p value 0.003). As in other studies like Waden J et al [11], Muggeo M et al [12], Barak Gaster, Irl Hirsch [13]our study also showed that poor glycemic control in Type 2 Diabetics with Microalbuminuria was associated with greater predisposition for Silent Myocardial Ischemia.

The Present study showed that in subjects of more than 60 years of age, 5 out of 7 (71 .4%) patients had a positive treadmill test and in patients in age group of 51-60 years of age,15 out of 22 (68%) patients had a positive treadmill test. The result is statistically significant.(p value is 0.002) and shows that increasing age itself is a risk factor for development of Silent Myocardial Ischemia.

In this study 82 % patients with microalbuminuria had developed diabetic retinopathy. Similar results were observed in other studies conducted by P.G. Raman et al [14], Wirta O [15], Moriya T etal [16] ,Yurong Zhang et al[17] and BasantPawar et al.[18] . In the present study, 68.75 % of proliferative diabetic retinopathy patients and 64 % of Non Proliferative Diabetic Retinopathy patients had positive treadmill test . Hence, we can deduce from the present study that diabetic retinopathy in Type 2 diabetics with microalbuminuria is associated with greater predisposition for silent myocardial ischemia.

In this study it was observed that 64% of asymptomatic Type 2 DM patients with microalbuminuria had Silent myocardial ischemia. On statistically analyzing the result it was found to be statistically significant as evidenced by a (p value is <0.005).These results are similar to those observed in other studies conducted by (Martin K et al [19], McCombetet al [20] , Abdul Zahrah F et al [21] , Dinneen SF [22] et al and Valmadrid CT et al. [23]). Hence we can deduce from this study that microalbuminuria is an important risk factor for development of silent myocardial ischemia in asymptomatic patients of type 2 Diabetics.

7. Conclusions

In the present study, 64 % of asymptomatic patients with microalbuminuria had a positive treadmill exercise test. The prevalence of microalbuminuria increased with worsening glycemic control, with increasing duration of diabetes and with increase in BMI. Hence it is suggested from this study that microalbuminuria is an independent risk factor for development of silent myocardial ischemia. Early detection of microalbuminuria can help in screening and identification of a subset of patients who are predisposed to develop silent myocardial ischemia and thus can be very helpful in preventing future silent myocardial infarctions and their associated mortality and morbidity.

8. Limitations

Larger multicentric studies with bigger sample size are needed to get to some definite conclusion. Small sample size was a limitation of this study. The reasons were varied. Reluctance of asymptomatic patients to undergo a exercise stress test was the biggest hindrance to increase the sample size. Also hypertensive patients were excluded from the study to limit the confounders for microalbuminuria. Thus a larger number of patients could not be enrolled in the study.

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