

## Original Research Article

# The study of correlation of silent myocardial ischemia with microalbuminuria in patients of type 2 diabetes mellitus

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## ABSTRACT

**Background:** Diabetes is a common and serious disease leading to chronic, mostly irreversible macro and microvascular complications.

**Methods:** 50 Patients, attending Diabetic OPD at SGRD hospital, Amritsar. Asymptomatic patients with no symptoms or history of IHD and normal ECG with microalbuminuria were enrolled in the study. A complete clinical examination was done.

**Results:** The prevalence of microalbuminuria increased with worsening glycemic control, as evidenced by prevalence of 74 % in patients with HbA1c of more than 9 percent. The prevalence of microalbuminuria increased with the duration of diabetes, as evidenced by prevalence in 48 % in patients, with duration of diabetes of more than 11 years. The prevalence of microalbuminuria increased with increased BMI, as evidenced by prevalence of 56 % in overweight Patients. The prevalence of microalbuminuria increased in patients of Diabetic Retinopathy, as evidenced by prevalence of 82 % in patients of Diabetic Retinopathy. In the present study, 70.8 % patients with duration of diabetes in the range 11-15 years had positive treadmill test.

**Conclusions:** Hence, in this study it was observed that longer the duration of diabetes with microalbuminuria, greater is the predisposition for silent myocardial ischemia. In the present study, 64 % of asymptomatic patients with microalbuminuria had a positive treadmill exercise test. Hence, we deduce from this study that microalbuminuria is an independent risk factor for silent myocardial ischemia.

**Keywords:** Microalbuminuria, Silent myocardial ischaemia, Type 2 diabetes mellitus

## INTRODUCTION

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, is often asymptomatic and silent and may present without warning as Acute Myocardial Infarction, Heart Failure, Arrhythmia or sudden death.<sup>1</sup> Microalbuminuria (MA) 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.<sup>2</sup>

Microalbuminuria has been defined by consensus, based on risk of renal disease, as a urinary albumin excretion rate between 30 and 300 mg/day.<sup>3</sup> 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.<sup>4</sup> Therefore,

patients with diabetes should be screened regularly for microalbuminuria.<sup>4</sup>

## METHODS

The aims and objectives of the study was to study the correlation of Silent Myocardial Ischemia (as detected by abnormal exercise stress test) with Microalbuminuria in patients of Type 2 diabetes mellitus. To study the correlation of Silent Myocardial Ischemia with duration of diabetes in patients of Type 2 diabetes mellitus having Microalbuminuria. To study the correlation of Silent Myocardial Ischemia with the level of glycemic control in patients of Type 2 diabetes mellitus having Microalbuminuria. To study the correlation of Silent Myocardial Ischemia with the Diabetic Retinopathy, seen in patients of Type 2 diabetes mellitus having Microalbuminuria. To study the correlation of Silent Myocardial Ischemia with Body Mass Index in patients of Type 2 diabetes mellitus having Microalbuminuria.

Study design: A Prospective Hospital based Study. Source of data: Type II diabetic patients attending the Diabetic OPD at SGRD Hospital, a Tertiary Care Hospital, for the duration period of 11/2 years. Sample size: 50 Patients, attending Diabetic OPD at SGRD hospital, Amritsar.

### Inclusion criteria

- All patients diagnosed with Type II diabetes as per the ADA guidelines.
- Age 30 years to 65 years, both males and females.
- Patients who were voluntarily willing to participate in the study after informed consent.

### Exclusion criteria

- Patients with active chest pain or any history of IHD or its Treatment,
- Hypertension,
- Type 1 DM or any other form Diabetes Mellitus eg. MODY, LADA,
- Thyroid disease,
- Nephrotic syndrome,
- Any acute illness including UTI,
- Abnormal ECG,
- Any contraindication for treadmill stress test,
- Patients on angiotensin converting enzyme inhibitors,
- Patients on angiotensin receptor blockers,
- Pregnant woman,

### Data collection

Detailed history, examination, fundus and investigations eg; ECG, microalbuminuria Fasting and Post Prandial Blood Sugar, HbA1C, Sr. Creatinine were done after

informed consent. 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.

**Table 1: Body mass index (BMI) was accordingly categorized.**

Type	BMI (kg/m <sup>2</sup> )
Underweight	<18.5
Normal	18.5-24.9
Overweight	>25

## RESULTS

All the above-mentioned data was meticulously collected and statistically analyzed.

**Table 2: Distribution of data by age group.**

Age group	Number of cases	%
< 40	6	12
41-50	15	30
51-60	22	44
>61	7	14
Total	50	100

In the present Study, majority of the patients were between the age group of 51 to 60 years.

**Table 3: Distribution of data by sex.**

Sex	Number of cases	%
Male	30	60
Female	20	40
Total	50	100

In the present study, 60% of the patients were Males and 40 % were Females.

**Table 4: Distribution of data by HBA1C.**

HBA1C	Number of cases	%
< 7	6	12
7-9	15	30
>9	29	58
Total	50	100

**Table 5: Distribution of data by duration of diabetes mellitus.**

Duration of DM	Number of cases	%
< 5	8	16
6-10	20	40
11-15	24	48
Total	50	100

In the present study, most of the patients (58%) were having a HbA1C of more than 9 percent. In the present study, most patients had history of Diabetes for more than 10 years (44%).

**Table 6: Distribution of data by BMI.**

BMI	Number of cases	%
Under weight	2	4
Normal	20	40
Overweight	28	56
Total	50	100

**Table 7: Distribution of data by funduscopy.**

Fundus	Number of cases	%
Normal	9	18.0
NPDR	25	50.0
PDR	16	32.0
Total	50	100

In the present study, most of patients the patients (58%) were overweight.

In the present study, 82% of the patients were having Diabetic Retinopathy.

**Table 8: Correlation of silent myocardial ischemia in asymptomatic patients of type 2 diabetes mellitus with microalbuminuria.**

Stress test	No. of cases	%	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 the patients had a Positive stress test.

**Table 9: Correlation of silent myocardial ischemia in asymptomatic type 2 diabetic patients with age.**

Age group	Total number of cases	No. of positive cases	% of positive cases	Chi-value	P – value	Result
< 40	6	2	33.33	13.418	0.012	Not significant
41-50	15	10	66.67	15.845	0.002	Significant
51-60	22	15	68.18	19.548	0.001	Significant
>61	7	5	71.43	20.607	0.000	Highly significant
Total	50	32				

P < 0.05 = Significant, P > 0.05 = Not Significant

In patients more than 60 years of age 5 Out of 7 (71.4%) had a Positive Treadmill Test. In patients from 51-60

years of age 15 out of 22 (68%) had a Positive Treadmill Test.

**Table 10: Correlation of silent myocardial ischemia in asymptomatic type 2 diabetic patients with sex.**

Sex	Total no. of cases	No. of positive cases	% of positive cases	Chi-value	P – value	Result
Male	30	22	73.33	15.712	0.000	Highly significant
Female	20	10	50	3.742	0.148	Not significant
Total	50	32				

P < 0.05 = Significant. P > 0.05 = Not Significant.

In the present study, 22 out of 30 (73 %) Males had Positive Stress test as compared to 10 out of 20 (50%) females.

## DISCUSSION

Diabetes has reached epidemic proportions worldwide. Microalbuminuria marks the onset of endothelial

dysfunction in Diabetes. Microalbuminuria is increasingly being recognized now as a cardiovascular risk marker.<sup>5</sup> To target preventive strategies, risk stratification of the population has to be effective. In the present study 50 asymptomatic Type 2 Diabetics with microalbuminuria were subjected to exercise stress test to see for silent myocardial ischemia.

**Table 11: Correlation of silent myocardial ischemia in asymptomatic type 2 diabetic patients with glycemic control.**

Hba1c	Total no. of cases	No. of positive cases	% 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				

P < 0.05 = Significant. P > 0.05 = Not Significant.

**Table 12: Correlation of silent myocardial ischemia in asymptomatic type 2 diabetic patients with duration of diabetes.**

Duration of DM	Total no. of cases	No. of positive cases	% 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

P < 0.05 = Significant. P > 0.05 = Not Significant.

In the present study, most of the patients, 25 out of 29 (86 %) with Hba1c > 9 had Positive Treadmill Test.

In the present study, 17 Out of 24 (70.8 %) patients with history of Diabetes more than 10 years had a Positive Treadmill Test.

**Table 13: Correlation of BMI with silent myocardial ischemia in asymptomatic type 2 diabetics with microalbuminuria.**

BMI	Total number of cases	Number of positive cases	Percentage of positive cases	Chi-value	P – value	Result
Under weight	2	0	0	1.542	0.742	Not significant
Normal	20	9	45	11.470	0.002	Significant
Over weight	28	23	82.14	31.540	0.001	Highly significant
Total	50	32				

P < 0.05 = Significant. P > 0.05 = Not Significant.

**Table 14: Correlation of silent myocardial ischemia in asymptomatic type 2 diabetic patients with diabetic retinopathy.**

Fundus	Total number of cases	Number of positive cases	Percentage of positive cases	Chi-value	P - value	Result
Normal	9	5	55.55	4.324	0.042	Significant
NPDR	25	16	64	24.350	0.001	Significant
PDR	16	11	68.75	27.854	0.000	Highly significant
Total	50	32				

P < 0.05 = Significant, P > 0.05 = Not Significant

In the present study, 23 out of 28 (82%) Overweight patients had a Positive Treadmill Test.

In the present study 11 Out of 16 (68.75 %) patients with Proliferative Diabetic Retinopathy had a Positive Treadmill Test. In the present study 16 Out Of 25 Patients (64%) with non-proliferative Diabetic Retinopathy had a Positive Treadmill Test.

### Demographic profile

#### Age

Increasing age is reported as one of the risk factors for the development of microalbuminuria.

**Table 15: Average age of patients with microalbuminuria in various studies.**

Study	Mean age in years
Seth J et al <sup>6</sup>	56.8
Taneja V et al <sup>7</sup>	58.37

In the present study, mean age of all subjects was found to be 51.6 years, which is quite similar to that, seen in other studies.

#### *Age risk factor for silent myocardial ischemia*

In the present study, shows that increasing age itself is a risk factor for development of Silent Myocardial Ischemia.

#### *Sex*

Mubarakali N et al in their study measured 24 hour urinary protein excretion in 152 diabetic subjects.<sup>8</sup> Microalbuminuria was diagnosed in 28% of the diabetic patients. The frequency of Microalbuminuria was higher in men (64%) than in women (36%). Meisinger C et al, observed 58% of the patients with microalbuminuria were males as compared to 42% females.<sup>9</sup> In the present study also we found that 60% patients with microalbuminuria were males and 40% were females, which is similar to that seen in other studies.

#### *Male sex risk factor for SMI*

In a cross-sectional analysis performed by Ferrara A et al, 157,458 found that, male sex was more predisposed to myocardial ischemia.<sup>10</sup>

In our study, male gender is an important risk factor for development of silent myocardial ischemia in type 2 Diabetics.

#### *Duration of diabetes and silent myocardial ischemia*

In a study done by Patel et al, the authors showed that the prevalence of microalbuminuria increased progressively with the duration of diabetes.<sup>11</sup>

**Table 16: Mean duration of diabetes with microalbuminuria in various studies.**

Study	Duration in years
Mongensen CE et al <sup>12</sup>	14.8±4.4
Patel et al <sup>11</sup>	10.3±5.82
J.Sheth et al <sup>13</sup>	8.57±3.89
Lamba IMS. et al <sup>14</sup>	12.57±6.3
Present study	11.7±5.0

Similar to other studies, in the present study it was found to be 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.

#### *Glycaemic control and silent myocardial ischemia*

Waden J et al found increasing impairment of glycemic control detected by rising level of HbA1c in patients with Type 2 Diabetes Mellitus with Microalbuminuria is associated with greater predisposition for silent myocardial ischemia.<sup>15</sup> Muggeo M et al in the Verona Diabetes study found long-term instability of fasting plasma glucose an independent cardiovascular risk factor in type 2 diabetics.<sup>16</sup> In our study 25 out of 29 (86.2%) patients with HbA1c > 9 had positive treadmill test. This was statistically significant (p value 0.003).

#### *Microalbuminuria, diabetic retinopathy and silent myocardial ischemia*

Wirta O et al in their study observed that 26 % patients with normoalbuminuria had diabetic retinopathy as compared to 62% in patients with microalbuminuria.<sup>17</sup> Moriya Tet al in their study found that Microalbuminuria was present in 82%.<sup>16</sup> Patients with diabetic retinopathy. In our study 82 % patients with microalbuminuria were having Diabetic Retinopathy. Similar to the results of other studies as noted above, this study also points to the fact patients with microalbuminuria have increased incidence of Diabetic retinopathy. The result is statistically significant (p value is 0.005).

#### *Silent myocardial ischemia in type 2 diabetics*

Achari et al in a study of 120 asymptomatic type 2 diabetic patients assessed for presence of silent ischemia by a standard treadmill test by using the Bruce protocol.<sup>19</sup> The author found that 51 (42.5%) had evidence of myocardial ischemia. In another study by Garg PK et al who studied 40 patients of type 2 diabetes mellitus and compared them with 30 healthy controls.<sup>20</sup> All subjects underwent exercise test (bicycle ergometry). It was found that prevalence of silent myocardial ischemia was 3.3 times higher in patients of Type 2 DM.

#### *Microalbuminuria and silent myocardial ischemia*

Martin K et al studied the correlation of Silent myocardial ischemia (SMI) and microalbuminuria in subjects with Type 2 diabetes.<sup>21</sup> 52% patients had Silent myocardial ischemia during treadmill testing. Further detailed analysis showed that Coronary Artery Disease events were also significantly related to Microalbuminuria.

Another similar study conducted by McComb et al compared the prevalence and severity of Silent myocardial ischemia in asymptomatic Type 2 DM patients with and without microalbuminuria.<sup>22</sup> Patients with microalbuminuria had a higher prevalence of ischemic response (>1mm ST depression) (65% vs 40%,

$p=0.016$ ), reduced total exercise time (5 vs 7 minutes  $p<0.001$ ), reduced work (6 vs 8 METs,  $p<0.001$ ). In these subjects, the higher prevalence of ischemic response at low workloads suggests a higher probability of future coronary events. On further analysis, albumin excretion rate was shown to be the strongest independent predictor of ischemic response. This study concluded that silent myocardial ischemia is more common in asymptomatic Type 2 DM patients with microalbuminuria.

In the present study we found that in our study group, 64% of asymptomatic Type 2 DM patients with microalbuminuria had positive stress test, implying Silent myocardial ischemia. It was statistically significant.

## CONCLUSION

In the study group microalbuminuria was present in 60% Males and 40% Females patients. The prevalence of microalbuminuria increased with worsening glycemic control, as evidenced by prevalence of 74% in patients with HbA1c of more than 9 percent. The prevalence of microalbuminuria increased with the duration of diabetes, as evidenced by prevalence in 48% in patients, with duration of diabetes of more than 11 years. The prevalence of microalbuminuria increased with increased BMI, as evidenced by prevalence of 56% in overweight Patients. The prevalence of microalbuminuria increased in patients of Diabetic Retinopathy, as evidenced by prevalence of 82% in patients of Diabetic Retinopathy. In the present study, 64% of asymptomatic patients with microalbuminuria had a positive treadmill exercise test. Hence, we deduce from this study that microalbuminuria is an independent risk factor for silent myocardial ischemia. In the present study, 73% males with microalbuminuria had a positive treadmill exercise and 50% female patients with microalbuminuria had a positive treadmill exercise test. Hence, we deduce from this study Type 2 diabetic males with microalbuminuria are associated with greater predisposition for silent myocardial ischemia than the females. In the present study, 71% of patients in the age group of 60 years and above with microalbuminuria had a positive treadmill exercise test. This shows that increasing age is associated with greater predisposition for silent myocardial ischemia in type 2 diabetic patients with microalbuminuria. In the present study, 86.2% patients with HbA1C  $>9\%$  had positive treadmill test. Hence in this study it was observed that poor glycemic control is associated with greater predisposition for silent myocardial ischemia in type 2 diabetic patients with microalbuminuria. In the present study, 70.8% patients with duration of diabetes in the range 11-15 years had positive treadmill test. Hence in this study it was observed that longer the duration of diabetes with microalbuminuria, greater is the predisposition for silent myocardial ischemia. In the present study, 82% of obese, 45% of normal and none of the underweight patients had positive treadmill test. In this study it was observed that increasing BMI in type 2

diabetics with microalbuminuria is associated with greater predisposition for silent myocardial.

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