IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 11 Ver. VI (November. 2016), PP 16-19
www.iosrjournals.org

Correlation of Severity of Left Ventricular Dysfunction with Duration of Disease in Type 2 Diabetes Mellitus with Microalbuminuria

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Abstract:
Background*: To study the left ventricular(LV) function in patients with Type 2 Diabetes Mellitus (DM) with microalbuminuria and find out if any correlation exists between LV dysfunction and duration of diabetes.*
Methods*: In this observational study Type 2 DM patients fulfilling the inclusion and exclusion criteria were subjected to Micral Test. Echocardiographic assessment was done using standard criteria in those patients who were positive for microalbuminuria . Left ventricular systolic as well as diastolic function was assessed and the data statistically analysed for any significant correlation with duration of diabetes.*
Results: *62 patients out of 251 selected Type2 DM patients were positive for microalbuminuria with a male to female ratio of 1.7:1.The age range in the study group was 46-66 yrs(mean 53.7 yrs).The duration of disease among the subjects was between 9-18 yrs.(mean=14.5 yrs). Mean BMI in the group was 27.17 (21.05-36.89). The mean values of lipid profile were Total cholesterol-217 mg/dl, TG-188 mg/dl,HDL-29.4 mg/dl,LDL-159 mg/dl and VLDL-60 mg/dl. Patients with microalbuminuria in the range of 20mg/L, 50 mg/L, 100mg/L and 150 mg/L were18%,31%,40% and 11% respectively.LV diastolic and systolic dysfunction was observed in 46% and 19% of patients respectively.Global LV dysfunction was noted in 11% of subjects and 24% of cases had no LV dysfunction. Depending on the level of microalbuminuria(from 20mg/L to 150mg/L) the mean value of Ejection fraction(EF) was from 61.12±5.11 to43.00±2.16 and cardiac output was 4.11±0.27 to 3.11±0.4.Ejection fraction and fractional shortening showed significant correlation with duration of disease with p values <0.01 each.E-point septal separation and cardiac output changes were having no significant correlation. Similarly, IVRT and deceleration time showed significant correlation with duration of diabetes(p<0.01) whereas E/A did not show statistically significant correlation with disease duration.*
Conclusion: *Left ventricular dysfunction occurs in Type 2 DM with microalbuminuria and the severity of dysfunction correlates well with duration of diabetes in patients with microalbuminuria.*
Keywords*: Type 2 DM, Cardiomyopathy, Diastolic dysfunction, Systolic dysfunction, Microalbuminuria.*

I. Introduction

Diabetes Mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] The hyperglycemia of diabetes mellitus is the result of either absolute or relative insulin deficiency arising from insulin resistance or progressive deterioration of beta cells function. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1] Diabetes mellitus has become a global epidemic with increasing prevalence worldwide especially for populations in Asia and among young people. Worldwide the prevalence of DM is estimated to increase from 382 million in the year 2013 to 592 million by the year 2035[2].This rise in the prevalence is mostly due to the rise in the incidence of Type 2 DM which represents about 90-95% of the disease burden. The population in India has an increased susceptibility to DM. During the year 2004 there were an estimated 37.7 million cases of diabetes in India, of these 21.4 million were in urban areas and 16.3 million were in rural areas.[3]

Cardiovascular disease is the major reason for morbidity and mortality among patients with diabetes. Many aspects of heart disease in patients with diabetes are secondary to atherosclerosis i.e., macrovascular disease. But the mechanism of some of the myocardial pathologies in diabetes have obvious similarities to mechanisms of complications in other organs, e.g in the kidney[4]. Studies have found that diabetes mellitus produces functional, biochemical and morphological abnormalities independent of coronary atherosclerosis and hypertension. These abnormalities may result in impaired left ventricular diastolic dysfunction contributing importantly to heart failure with normal systolic function[5]. Duration and degree of hyperglycemia correlates with complications in diabetes. In our study we have tried to find out the correlation between duration of diabetes and one of the significant late complications i.e., left ventricular dysfunction.

II. Material and Methods

The study was carried out over a period of 2 years as a prospective observational study. Cases of Type 2 DM were selected both from Out-patient Dept. as well as from the Wards. Cases were diagnosed according to the diagnostic criteria of ADA-2000. Both newly diagnosed and follow up cases of Type 2DM were considered for the study. Those patients with hypertension , Ischemic heart disease, valvular heart disease, chronic renal failure, anemia and overt protienuria were excluded from the study. After exercising exclusion criteria a total of 251 subjects were selected for detection of microalbuminuria by Micral Test. Micral Test is a semiquantitative immunologic dipstick test manufactured Boehringer Mannhein Ltd. Which gives immediate and reliable semiquantitative estimate of microalbuminuria in urine with a sensitivity and specificity level of 96.7% and 71% respectively.

Subjects with microalbuminuria were taken for the final study. Detailed history was taken , meticulous physical examination including fundoscopy done and relavant investigations were carried out and data recorded in a case report form. Echo-cardiographic assessment of left ventricular function(2D and M mode) was one with commercially available ultrasound system (HDI 1500). All recordings and observations were performed by the same person as per the recommendations of American society of Echocardiography. Criteria of American society of Echocardiography were used for assessing LV systolic dysfunction. The parameters considered were LV ejection fraction less than 50%, Percentage fractional shortening less than 36%, E-point septal separation more than 7 mm and cardiac output less than 3 lit/min. Mayo clinic criteria were used for detecting LV Diastolic dysfunction. The parameters considered for LV diastolic dysfunction were A velocity higher than E velocity on PW mitral Doppler, A/E ratio greater than 1, Deceleration time more than 240 m sec on dual M-mode echo of aortic and mitral valve recorded simultaneously.

The recorded and calculated data were analysed using Microsoft Excel statistical software. Linear regression method was used to find out correlation among variables. Significance between different groups and means were calculated by using Students T-test.

III. Result

After exercising the inclusion and exclusion criteria, a total of 251 cases of Type 2 diabetes were considered for detection of microalbuminuria by Micral Test out of which 62 cases showed positive result and were taken up for final study. The male to female ratio in the subjects (n=62) was 1.6:1.There was no significant sex difference in the prevalence of microalbuminuria. In the study group, the age range was 46-66 years with a mean age of 53.7 years.The duration of the disease in the study population was from 9 to 18 years with a mean duration of 14.5 years. Majority of the study population (38.8%)were having duration of disease more than 16 yrs. Subjects with duration of disease between 9 to 12 years and 13 to 16 yrs were in equal numbers (30.6% each).The BMI in the study population was in the range of 21.05 to 36.89 (mean 27.17). The mean values of lipid profile were LDL- 159 mg/dl, TG -188mg/dl,HDL-29.4mg/dl which shows an atherogenic lipid profile in the subjects. Majority of the study subjects were having moderate range microalbuminuria (50 mg/L and 100 mg/L combindly accounting for 71% of cases.) Subjects with microalbuminuria of <20 mg/L were 18% and >150 mg/L were 11% only. Left ventricular dysfunction was noted in 76% of subjects and most of the subjects (46% of total cases) were having diastolic dysfunction. Number of cases with left ventricular systolic or diastolic dysfunction were maximum at albuminuria range of 50 mg/L.

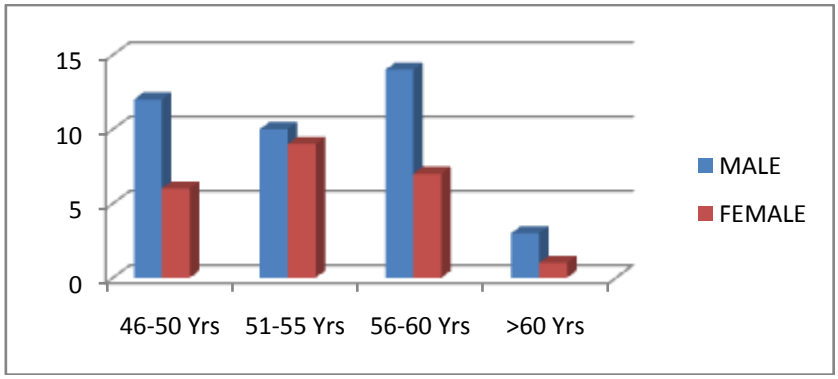

Fig.1 Age and sex distribution of study group (n=62)

Microalbuminuria in mg/L	Mean duration of diabetes in yrs
20	12.71±3.2
50	14.6±3.13

100	15.3±2.17
150	16.29±1.1

Table 1 showing severity of microalbuminuria and duration of diabetes (r=0.393,p<0.01,df=60)

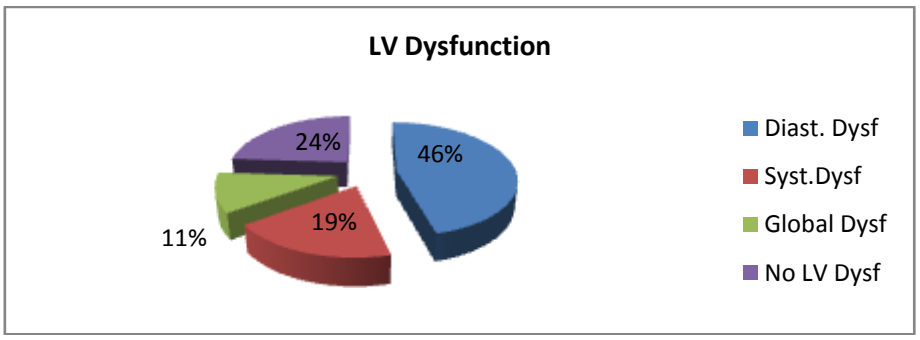

Fig 2: LV Dysfunction among study population

Parameters of LV Dysfunction	Duration of diabetes among study group in years			p value
	9-12	13-16	>16	
EF±SD	59.00±7.97	52.4±9.51	52.1±8.38	<0.01
FS±SD	41.24±6.23	37.8±4.14	37.4±3.91	<0.01
EPSS±SD	6.69±1.76	7.6±2.75	7.9±2.18	>0.05
CO±SD	3.92±0.54	3.59±0.62	3.48±0.61	>0.05
IVRT±SD	104.79±9.09	115.79±8.03	115.08±6.99	<0.01
DT±SD	232.63±12.55	245.15±13.04	245.73±5.25	<0.01
A/E±SD	0.91±0.14	1.04±0.15	1.03±0.16	>0.05

Table 2 showing the parameters of LV Function with duration of diabetes

As shown in the Table 1,severity of microalbuminuria is increasing from 20mg/L to 150 mg/L with increase in mean duration of disease which is statistically significant(p<0.01).Table 2 shows that the mean value of ejection fraction is decreasing from 59.00±7.97 to 52.1±8.38 with increasing duration of diabetes from 9-12 yrs to >16 yrs. The fractional shortening is also decreasing from 41.24±6.23 to 37.4±3.91. The correlation between decreasing Ejection fraction and fractional shortening (which are parameters of left ventricular systolic function) with increasing duration of disease, were found to be statistically significant(p<0.01). But other two parameters of LV systolic function like EPSS and cardiac output though deteriorating in values but do not have any significant correlation with increasing duration of diabetes.

Similarly the parameters of diastolic function were also found to be deteriorating with increasing duration of diabetes among the study population. Mean value of Isovolumetric relaxation time (IVRT) was increasing from 104.79±9.09 to115.08±6.99 with increasing duration of disease and Decelaeration time increasing from232.63±12.55 to 245.73±5.25 and both the changes are statistically significant(p<0.01). Though the A/E value was observed to be increasing with duration of diabetes mellitus it was not statistically significant.

IV. Discussion

Cardiovascular diseases are the leading cause of death among individuals with diabetes mellitus. Individuals with Type 2 DM have three to four fold increased risk of cardiovascular disease related mortality when compared with healthy counterparts[6]. Patients with diabetes have a high prevalence of chronic heart failure and a high incidence of heart failure and re-infarction after acute myocardial infarction. These cannot be explained by more extensive coronary atherosclerosis, a higher prevalence of hypertension or larger infarcts in this population than in people without diabetes. Myocardial disease in diabetes is not a microvascular disease in true sense, yet there are conspicuous similarities in the diabetic heart and traditional microvascular complications on both pathoanatomic and molecular levels, especially with regard to the production of extracellular matrix as in the diabetic kidney[4]. Diffuse cardiac fibrosis is observed in diabetes and may contribute to diastolic dysfunction. Similar to the pathology of the diabetic kidney, the amount of extracellular matrix is increased in the diabetic heart.

Left ventricular function in Type 2 DM patients has been investigated by various researchers [7-10] and all have reported LV dysfunction of variable extent. Rao M S et al in their study comprising of 30 adult Type 2 DM cases observed the left ventricular diastolic and systolic dysfunction in 56% and 23% cases[11]. Zabalgotia M et al in their study of 86 normotensive Type 2 DM cases reported LV diastolic dysfunction in 47% cases[12]. In our study we observed both diastolic and systolic dysfunction(46% and 19% respectively) which is similar to observations of other workers like Rao M S et al.

Duration of DM and degree of glycemic control are the best predictors of the development retinopathy. Going by the above description, Myocardium is anticipated to undergo similar functional deterioration with duration of diabetes. Shapiro L M et al in their study have observed that abnormalities of left ventricular function are related to the duration of disease[13]. Rao M S et al have also observed similar findings in their study. In our study we have observed left ventricular systolic as well as diastolic dysfunction in our cases which is further deteriorating with increasing duration of disease. This is in accordance with the observations of Shapiro L M et al and Rao M S et al.

Various researchers have observed that with increasing duration of diabetes severity of microalbuminuria also increases.Y M Smulders et al [14]in their study have concluded that microalbuminuria progresses linearly with time.Raman et al have microalbuminuria in 68% cases with disease duration more than 25 years.In our study we have observed that with increasing duration of disease microalbuminuria severity also increasing which is statistically significant.

Microalbuminuria is a marker of widespread microangiopathy . A strong correlation between severity of microalbuminuria and left ventricular dysfunction has been well established by various studies [15-18]. Various parameters of left ventricular function have been reported to deteriorate with increasing severity of microalbuminuria.

The association of microalbuminuria with left ventricular dysfunction can well be explained by the fact that microalbuminuria reflects renal and systemic transvascular albumin leakage that is perhaps due to low vessel wall content of heparan sulphate that has been shown not only in glomerular basement membrane but also in coronary arteries. These tissue alteration can increase end diastolic myocardial stiffness as well as alter normal systolic function. All these changes progress with time and can explain the phenomenon of increasing LV dysfunction with increasing duration of diabetes.

V. Conclusion

Diabetes mellitus is sometimes considered as a vasculopathy affecting microvasculature in different organs and accelerates atherosclerosis in larger vessels. Microalbuminuria is marker of widespread endothelial dysfunction and predicts complications in different organs including myocardium. Cumulative exposure to hyperglycaemia is strongest risk factor in progression of long term diabetic complications. Along with severity of hyperglycemia, duration of diabetes is also an important predictor of chronic complications like diabetic cardiomyopathy.

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