

## Diabetic cardiomyopathy in Manipur

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### ABSTRACT

**Objective:** To assess the prevalence of diabetic cardiomyopathy in patients with diabetes mellitus in Manipur and its correlation with different parameters like obesity, blood pressure, lipids, duration of diabetes, and glycemic control. **Materials and Methods:** A total of 100 type 2 diabetic patients were selected randomly. Anthropometric parameters were recorded, blood glucose levels and lipid profiles were determined, and the echocardiographic examinations were performed in all patients according to standard techniques. Ejection fraction (EF) was calculated by the formula  $LVEF\% = \frac{(LVID)2 - (LVIDS)2}{(LVID)2 - (LVIDS)2}$ . Left ventricular EF was considered normal when EF was 55 to 75%. Diastolic dysfunction was calculated by measuring E and A transmitral inflow velocity. Left ventricular mass in grams is calculated by the formula  $LVM (gm) = 1.04 \times 0.8 [(LVID + PWT + IVST)^3 - LVID^3] + 0.6$ . **Results and Conclusions:** Diabetic cardiomyopathy was found in 40 patients (40%) of the total study, 29 males (44.6%) and 11 females (31.4%).

**Key words:** Diabetic cardiomyopathy, echocardiography, type 2 diabetes mellitus

### INTRODUCTION

A number of clinical, epidemiological, and pathological studies attribute the increased occurrence of clinical congestive heart failure in diabetic subjects to diabetic cardiomyopathy.<sup>[1]</sup> The Danish internist Lundback<sup>[2]</sup> proposed the term “diabetic cardiomyopathy” following the increased susceptibility of diabetic patients to heart failure and attributed it to a diabetes-specific myocardial disease. The entity was originally described in 1972 on the basis of observations in four diabetic patients who presented with heart failure without evidence of hypertension, coronary artery disease, and valvular heart disease.<sup>[3]</sup>

Diabetic cardiomyopathy in diabetic subjects can take the form of diastolic and/or systolic left ventricular dysfunction.<sup>[4,5]</sup> The mechanism of which are proposed to

the deleterious effects of hyperglycemia, hypertension, and impaired endothelial function. Microangiopathic changes in small vessels of the heart of diabetic patients may contribute to diabetic cardiomyopathy. An increase in left ventricular mass in diabetic patients have also been reported and diabetic women tend to have a much greater ventricular mass and increase in left ventricular wall thickness and chamber size.<sup>[6]</sup> Other abnormalities noted in diabetic heart include microvascular constriction, interstitial fibrosis, and edema.<sup>[7]</sup>

Clinically apparent diabetic cardiomyopathy may take years to develop, but echocardiography can detect significant abnormalities well before the onset of symptomatic heart failure. Early abnormalities are defined by the preserved left ventricular ejection fraction (EF) with reduced early diastolic filling. The diastolic dysfunction precedes systolic dysfunction in diabetic cardiomyopathy even before the presence of pathological findings on clinical examination.<sup>[8-10]</sup> When ventricular relaxation is impaired, early diastolic filling decreases progressively and a vigorous compensatory atrial contraction (“atrial kick”) occurs. With further disease progression, left ventricular compliance becomes reduced and filling pressures begin to increase. Systolic dysfunction occurs late when patients have already developed significant diastolic dysfunction.<sup>[11]</sup>

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The prevalence of diabetic cardiomyopathy varies between 20 to 40% according to different workers. Several studies have shown a correlation between glycemic control and left ventricular diastolic dysfunction,<sup>[12-14]</sup> whereas other studies have not found such correlation.<sup>[15,16]</sup> Ethnicity is believed to play a role in the development of heart failure, especially in association with diabetes. Diabetic cardiomyopathy was observed in white, black, and Hispanics but not among Chinese in the MultiEthnic Study of Atherosclerosis.<sup>[17]</sup> A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee revealed that the prevalence of heart failure was lowest in the Mexican-American subgroup followed by nonHispanic whites and African Americans.<sup>[18]</sup> Hispanics in America are more likely to have heart failure in relation with diabetes compared with the nonHispanics.<sup>[19]</sup> Manipur is a small state in the northeastern part of India which is ethnically different from the mainland India. To date, there has not been any study to evaluate the abnormalities of cardiac function in diabetic patients in the northeast India. This study was taken up to find out the prevalence of diabetic cardiomyopathy in patients with diabetes mellitus in Manipur and its correlation with different parameters like obesity, blood pressure, lipids, duration of diabetes, and glycemic control.

## MATERIALS AND METHODS

A total of 100 type 2 diabetic patients were selected randomly from the Diabetes Clinic, Regional Institute of Medical Sciences, Imphal, Manipur. Patients who were suffering from acute or chronic complications of diabetes, cardiovascular and respiratory diseases, liver disease, critical illness, chronic alcoholism, carcinoma, and any infection were excluded from the study.

A detailed history of the clinical information including the patient's age, gender, weight, height, and religion was noted. Blood glucose levels, fasting, postprandial, and random, and lipid profiles were determined according to standard procedures. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

### Echocardiography

The echocardiographic examinations were performed in all patients according to standard techniques<sup>[20]</sup> while the patients were lying flat or in the decubitus position by Siemens Simatic Versa plus Colour Doppler ultrasound machine. Left ventricular measurements were made with the Mmode beam positioned just beyond the mitral leaflets tips (mitral chordal level) perpendicular to the long axis of the ventricle. Standard echocardiographic measurements of diastolic and systolic left ventricular dimension left ventricle

internal dimension (LVID), posterior wall thickness (PWT), and interventricular septum (IVS) were measured from the leading edge to leading edge of each interface of intersect for optimal measurement accuracy.<sup>[21]</sup>

EF was calculated by the formula  $LVEF \% = (LVID)^2 - (LVIDS)^2$ . Left ventricular EF was considered normal when it was between 55 to 75%. Diastolic dysfunction was calculated by measuring E and A velocity across transmitral inflow velocity. Left ventricular mass in grams was calculated by the formula  $LVM (gm) = 1.04 \times 0.8[(LVID + IVST + PWT)^3 - LVID^3] + 0.6$ , where LVID is left ventricular end diastolic internal diameter; IVST, interventricular septal thickness; and PWT, posterior wall thickness.<sup>[22]</sup>

The diagnosis of diabetic cardiomyopathy is made according to the following echocardiographic criteria.<sup>[11]</sup>

- i. Diastolic dysfunction was defined as preserved left ventricle EF with (a) reduced early diastolic filling, (b) prolongation of isovolumetric relaxation, (c) increased atrial filling, the presence of which confirms diastolic dysfunction, (d) increased pre-ejection period (PEP) and shorter left ventricular ejection time (LVET) resulting in increases PEP/LVET ratio—an evidence of reduced left ventricular distensibility, and (e) left ventricular hypertrophy (LVH) on echocardiogram defined by an LV mass  $\geq 125 \text{ g/m}^2$  for men and  $\geq 110 \text{ g/m}^2$  for women.
- ii. Systolic dysfunction was characterized by reduced EF  $< 55\%$ .

Results were given as mean  $\pm$  SD. Means are compared by unpaired Students *t*-test. Chi-square or Fisher's exact test were used as appropriate. The observations and data were analyzed in the statistical package social sciences (SPSS). The level of significance was set at  $P < 0.05$ .

## RESULTS

Diabetic cardiomyopathy was found in 40 patients (40%) of the total study of 100 type 2 diabetic subjects comprising 29 males (44.6%) and 11 females (31.4%).

The age of diabetics with cardiomyopathy was found higher than those without cardiomyopathy ( $P < 0.397$ ). The duration of diabetes, blood pressure, and blood glucose levels were not significantly different between the cardiomyopathy and the non-cardiomyopathy groups, as shown in Table 1. The average BMI of all the patients with diabetes was 23. The diabetics with cardiomyopathy was found slightly more obese than those without cardiomyopathy ( $P < 0.5$ ).

Serum cholesterol was found higher among the diabetics

**Table 1: Clinical characteristics**

Clinical characteristics	DCM (n = 40)	Non DCM (n = 60)	P value
Age	60.325 ± 13.211	58.18 ± 11.79	0.3979
Sex (Male/Female)	29/11	36/24	
Duration in years	6.6 ± 2.372	6.91 ± 2.76	0.5624
BMI (kg/m <sup>2</sup> )	23.6 ± 2.687	23.26 ± 2.35	0.5050
Systolic BP (mmHg)	113.7 ± 37.046	123.86 ± 2.88	0.0365
Diastolic BP (mmHg)	76 ± 16.517	79.58 ± 22.83	0.3955
Random BG (mg%)	261.85 ± 107.235	259.36 ± 107.02	0.9096
Fasting BG (mg%)	140.925 ± 36.279	145.08 ± 42.55	0.6135
Postprandial BG (mg%)	287.7 ± 101.604	295.63 ± 100.09	0.7005
S. Cholesterol (mg%)	208.6 ± 145.852	173.15 ± 96.13	0.1458
S. Triglyceride (mg%)	156.025 ± 96.781	113.45 ± 68.44	0.0114
S. LDL (mg%)	102.8 ± 34.429	85.91 ± 32.07	0.0139
S. HDL (mg%)	36.8 ± 13.864	40.2 ± 13.07	0.2165

DCM: Diabetic cardiomyopathy, BMI: Body mass index, BP: Blood pressure, BG: Blood glucose, LDL-C: Low-density lipoprotein, HDL: High-density lipoprotein

with cardiomyopathy than those without cardiomyopathy although not statistically significant ( $P < 0.145$ ). Serum triglyceride and low-density lipoprotein (LDL) cholesterol were found significantly higher in the cardiomyopathy group ( $P < 0.011$  and  $P < 0.013$ ), whereas high-density lipoprotein (HDL) cholesterol was found lower among the diabetics with cardiomyopathy although not significantly ( $P < 0.216$ ).

Table 2 shows the echocardiographical characteristics of the study population. There were no significant differences in left ventricular septum (IVS), LVID between the diabetics with and without cardiomyopathy. A comparison of mean values of EF showed a significant reduction among the diabetic cardiomyopathies compared with those without cardiomyopathies ( $P < 0.001$ ); however, the fractional shortening was found slightly higher among the diabetics with cardiomyopathies than those without cardiomyopathy ( $P < 0.713$ ).

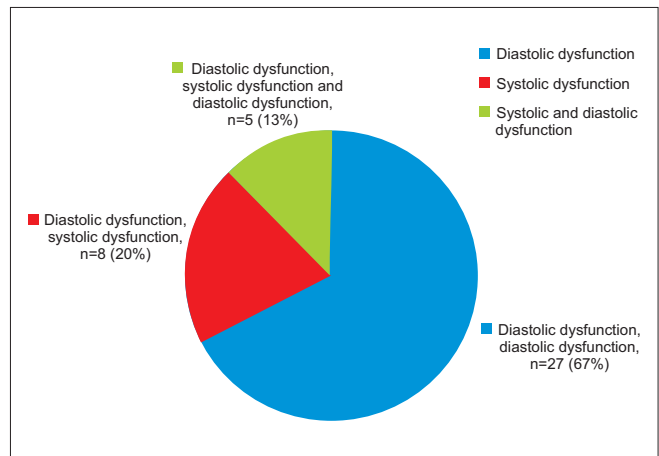
Left ventricular mass of the diabetic patients with cardiomyopathy ( $246.47 \pm 97$  g) was much higher than those without cardiomyopathy ( $187 \pm 7$  g;  $P = 0.0006$ ). Although the left ventricular mass was larger for both males and females in patients with diabetic cardiomyopathy, it was found much bigger in females than their male counterparts ( $284 \pm 136.8$  g vs  $232 \pm 76$  g;  $P < 0.133$ ), as shown at Figure 1.

Among the 40 patients with diabetic cardiomyopathy in our study, 67% had left ventricular diastolic dysfunction, 20% had systolic dysfunction, and 13% had both systolic and left ventricular diastolic dysfunction. The distribution between males and females also followed a similar pattern, as shown above in Figure 2. The incidence of diastolic dysfunction among diabetic cardiomyopathy was found to be higher than systolic dysfunction ( $P < 0.001$ ).

**Table 2: Echocardiographical characteristics**

	DCM (n = 40)	Non-DCM (n = 60)	P value
IVST (mm)	11.225 ± 3.99	10.7 ± 2.43	0.454
IVSes	13.7 ± 3.770	13.35 ± 2.94	0.604
LVPW (mm)	11.825 ± 4.684	11.2 ± 2.08	0.3654
LVPWes (mm)	14.92 ± 6.086	13.98 ± 1.93	0.2665
LVID (mm)	50.275 ± 10.536	48.7 ± 7.57	0.3865
LVIDes (mm)	44.25 ± 12.996	43.91 ± 14.55	0.9052
Ejection fraction (%)	52.1 ± 19.577	61.21 ± 7.60	0.0015
Fractional shortening (%)	34.075 ± 19.888	33 ± 8.91	0.7139
LV mass (mm)	246.475 ± 97.467	187 ± 69.78	0.0006

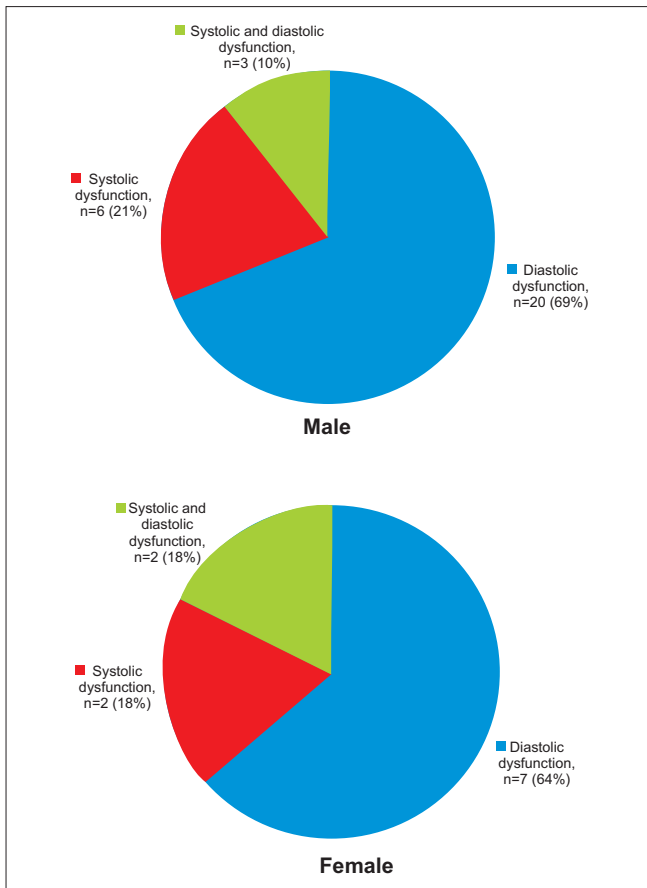
DCM: Diabetic cardiomyopathy, IVST: Inter-ventricular septum thickness, IVSes: Interventricular septum end-systolic dimension, LVPW: Left ventricular posterior wall thickness, LVPWes: Left ventricular posterior wall end-systolic dimension, LVID: Left ventricular internal dimension, LVIDes: Left ventricular internal dimension end systolic, LV Mass: Left ventricular mass

**Figure 1: Pattern of cardiac dysfunction in diabetic cardiomyopathy**

## DISCUSSION

Diabetic cardiomyopathy is a complex multifactorial disease initiated by hyperglycemia and changes in myocardial energy metabolism. Both processes increase oxidative stress and stimulate the protein kinase C and stress pathways leading to myocardial apoptosis, fibrosis, and inflammation. Abnormal calcium handling and shifts in myocardial expression impair excitation-contraction coupling. Autonomic neuropathy and decreased beta-adrenergic responsiveness lead to impaired regulation of excitation-contraction coupling. These changes are associated with extensive structural abnormalities. Clinically, the process manifests as an asymptomatic diastolic dysfunction, which progresses to symptomatic combined diastolic and systolic dysfunction.<sup>[11]</sup>

In our study, 40 patients (40%) of 100 type 2 diabetics had diabetic cardiomyopathy of which 67% had left



**Figure 2:** Pattern of cardiac dysfunction in diabetic cardiomyopathy in males and females

ventricular diastolic dysfunction, 20% left ventricular systolic dysfunction, and 13% had both. The incidence of left ventricular diastolic dysfunction among diabetic cardiomyopathy was found to be significantly higher than systolic dysfunction ( $P < 0.001$ ). Our findings are agreeable with that of Fang *et al.*<sup>[8]</sup> who observed higher number of left ventricular diastolic dysfunction of 29% compared with 24% left ventricular systolic dysfunction, and 17% of the diabetics in their study had both diastolic and systolic dysfunction. Schannwell *et al.*<sup>[9]</sup> and Di Banito *et al.*<sup>[10]</sup> reported that 30% of their well-controlled type 2 diabetic subjects had left ventricular diastolic dysfunction. Poirier *et al.*<sup>[2]</sup> observed left ventricular diastolic dysfunction in 60% of 46 well-controlled type 2 diabetic patients, of which 26% had pseudonormal filling pattern and 32% had impaired relaxation, a milder form of diastolic dysfunction in their study.

Our study did not find any correlation between BMI, blood pressure, duration of diabetes, and glycemic control with presence of diabetic cardiomyopathy, which was also observed by other workers.<sup>[2,14,15]</sup> Serum cholesterol, triglyceride, and LDL cholesterol levels were found

higher and serum HDL cholesterol was lower among the diabetics with cardiomyopathy compared with those without cardiomyopathy. Fang *et al.*<sup>[8]</sup> also did not find significant difference in diabetic duration, types and complications, hemoglobin A1c, blood glucose, and lipid profile, except LDL cholesterol between the diabetics with or without LVH. They observed a significantly greater LDL cholesterol in the diabetics with LVH than the diabetics without LVH ( $P = 0.019$ ).

EF among the diabetics with cardiomyopathy is significantly lower compared with the diabetics without cardiomyopathy ( $52.1 \pm 19.58\%$  vs  $61.2 \pm 7.6\%$ ,  $P < 0.001$ ) in our study. The left ventricular mass was more among the diabetics with cardiomyopathy compared with that of the diabetics without cardiomyopathy, which is statistically significant ( $P = 0.0099$ ) and this is consistent with the finding of other workers.<sup>[6,8]</sup> They opined that there is positive associations between heart weight and total fibrosis in patients with diabetes alone and with both diabetes and LVH. We also observed that although the left ventricular mass was larger both in males and females with cardiomyopathy, it was much more so among the diabetic females, which agrees with the findings of other workers.<sup>[7,11,23-25]</sup>

## CONCLUSION

Diabetic cardiomyopathy is a common complication in patients with type 2 diabetes which can be detected by echocardiography much before clinically obvious cardiac failure develops. Left ventricular diastolic dysfunction represents the first stage of diabetic cardiomyopathy followed by left ventricular systolic dysfunction. The study shows that serum cholesterol, triglyceride, and LDL cholesterol levels are higher and serum HDL cholesterol is lower among the diabetics with cardiomyopathy compared with those without cardiomyopathy. However, there is no correlation between obesity, blood pressure, duration of diabetes, and glycemic control with diabetic cardiomyopathy.

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