LEFT VENTRICULAR MASS INDEX IN NORMOTENSIVE TYPE 1 DIABETICS WITH DIABETIC NEPHROPATHY

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ABSTRACT

Asymptomatic cardiac disease is common in patients with diabetic nephropathy in absence of hypertension. Increased left ventricular mass (LVM) associated with nephropathy may contribute to increased cardiovascular risk and is an independent risk factor for sudden death. This study was undertaken to estimate the interrelationship between type I diabetes mellitus (DM), urinary protein excretion and left ventricular hypertrophy (LVH) expressed in terms of Left Ventricular Mass Index (LVMI).

In this hospital based, cross sectional, analytical study, 49 normotensive type I diabetics between 10 – 40 years age with proteinuria of varying degree were enrolled. Cases were analyzed in 3 groups as per proteinuria/day. Gr I < 30mg /d (n=18), Gr. II 30-300 mg/ dl (n=16) Gr. III > 300 mg /dl (n=15). Subjects with CAD (Coronary Artery Disease), hypertension, other cardiac disorders, CRF (Chronic Renal Failure), UTI (Urinary Tract Infection), COPD (Chronic Obstructive Pulmonary Disease) and pregnancy were excluded. Parameters like glycosylated Hb%., renal profile, retinopathy, LVM by 2D echo were assessed with various risk factors.

The mean LVMI was 115.4 gm/m^2 in Gr. III as compared to 90.99 gm/ m^2 and 71.98 gm/ m^2 in Gr. II and I which was statistically significant (P value <0.05). Mean IVS and LVPW thickness was found to be more in Gr. III (1.172$\pm$0.049, 1.112$\pm$0.073) as compared to Gr. II (1.106$\pm$0.094 and 0.978$\pm$0.05) and Gr. I (0.987$\pm$0.095 and 0.922$\pm$0.092) (P < 0.05). Proliferative retinopathy was found to be significantly associated with increased LVMI P < 0.05. Poor glycemic control (glycosylated Hb > 9%) was statistically significantly associated with increased LVMI (114.6$\pm$6.3) (P< 0.05). Duration of DM was found to be directly proportional to LVMI (P< 0.05).

Increased proteinuria was found to be directly associated with increased LVMI. Increased duration of DM, poor glycemic control and worsening retinopathy had significant positive correlation with increased LVMI.

KEY WORDS: Type 1 diabetes; Left ventricular mass index; Glycemic control; Retinopathy; Proteinuria.

INTRODUCTION

Heart disease occurs eventually in a majority of patients with diabetes mellitus (DM) and continues to be the outstanding factor in overall diabetic morbidity and mortality. About one–third of insulin dependent patients with established nephropathy die from cardiovascular causes (mainly ischemic heart disease) before they reach end stage renal failure (1, 2).

Asymptomatic cardiac disease is common in patients with diabetic nephropathy even in the absence of hypertension. The relative mortality from cardiovascular disease is, on average, increased 40-fold in type 1 diabetic patients with nephropathy compared with general population. The mortality from congestive heart failure and ischemic heart failure is 30-40 times higher for diabetic patients with clinical nephropathy than for those without (3).

Increased left ventricular mass (LVM) associated with nephropathy may contribute to the increased cardiovascular risk because left ventricular hypertrophy (LVH) is an ominous prognostic sign and an independent risk factor for sudden death, ventricular dysarrhythmia, myocardial ischemia, coronary heart disease and heart failure (4).

The relationship of left ventricular mass index (LVMI) with complications like nephropathy, retinopathy and other factors like duration of DM and glycemic control has been analyzed in the present study.

MATERIAL AND METHODS

In this hospital based, cross sectional, analytical study, 49 normotensive type 1 diabetes cases were enrolled. The subjects were categorized into three groups as per proteinuria (5) estimated by Micro protein Kit ERBA Test.

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Gr I : Proteinuria < 30mg/day (n=18)

Gr II : Proteinuria 30-300mg/day (n=16)

Gr III : Proteinuria >300mg/day (n=15)

Cases having ischemic heart disease, congenital heart disease, valvular heart disease, hypertension, acute complication of DM, urinary tract infection, pregnancy, COPD, CRF other than diabetic nephropathy were excluded from the study.

All the subjects were examined thoroughly. Glycosylated hemoglobin was estimated in all the cases by glycohemoglobin reagent test kit by PIONTE SCIENTIFIC INC. Patient was considered to have good glycemic control if glycosylated hemoglobin was <8%, fair if between 8 to 9% and poor if >9 (6).

2D echo was done in all the cases, various parameters like LV mass index, IVS, LV PW thickness and LV dimensions in systole and diastole were measured by Penn convention.

LV mass = $1.04 [(LVID Cd) + PWTd + SVTd)^3 – (WDd^3)]$-13.6gm

LVIDCd = Left ventricular internal diameter in diastole

PWTd = Posterior wall thickness in diastole.

S VTD = Inter ventricular septal thickness in diastole.

The left ventricular mass index was calculated by dividing left ventricular mass by body surface area. This index was used to adjust for variations in cardiac size that are attributable to difference in body size.

Statistical analysis was done by applying students t test. P value < 0.05 was considered to be significant.

RESULTS

49 cases were distributed as per proteinuria in 3 groups (Table 1). The mean LVMI was 115.4gm/m^2 in Gr. Ill as compared to 90.99 gm/m^2 and 71.98 gm/m^2 in Gr. II and I respectively which was statistically significant (P value <0.05) (Table 2). Mean IVS and LVPW thickness was found to be more in Gr. III (1.172±0.094 and 0.978±0.05) and in Gr. I (0.987±0.95 and 0.922±0.092) (p< 0.05).

Proliferative retinopathy was found to be significantly associated with increased LVM (P<0.05) (Table 3). Poor glycemic control (glycosylated Hb > 9%) was statistically significantly associated with increased LVMI (P <0.05) (Table 4)

Duration of DM was found to be directly proportional to LVMI (P<0.05) (Table 5)

Table 1: Distribution of Cases as per Proteinuria

Group	Urine Protein Exertion in mg/day	No. of cases n = 49
I	< 30	18 (36.73%)
II	30 – 300	16 (32.65%)
III	> 300	15 (30.61%)

In group I (n=18), duration of diabetes in 16 (88.88%) cases was <5 years, in 2 (11.11%) it was between 5 – 10 years and there were none with duration of more than 10 years. In group II (n=16), duration of diabetes in 4 (25%) cases was <5 years, in 11 (68.75%) it was between 5 –10 years and only one had >10 years. In group III (n=15), duration of diabetes in 7 (46.66%) cases was between 5–10 years and in 8 (53.33%) was more than 10 years.

In group I (n=18), 17 (94.44%) cases had good glycemic control, 1 (5.55%) case had fair glycemic control. None had poor glycemic control. In group II

Table 2: Relationship of Mean LVMI with Proteinuria in Various Groups

Group	Mean LVMI (gm/m^2)
I (n=18)	71.98 ± 6.54*
II (N=16)	90.99 ± 4.02*
III (N=15)	115.4 ± 9.32*
**P value*	*< 0.05*

Table 3: Relationship of Mean LVMI with Type of Retinopathy

Type of Retinopathy	Mean LVMI (gm/m^2)
N (n=22)	*77.1 ± 10.43
PP (n=18)	*97.72 ± 16.1
P (n=9)	*114.22 ± 11.28
**P value*	*< 0.05*

Table 4: Relationship of Mean LVMI with Glycemic Control (Glycosylated Hb%)

Glycemic Control (Gly Hb%)	Mean LVMI (gm/m2)
Good (£ 8) (n=28)	79.68 ± 7.95*
Fair (8.1 –9) (n=9)	97.31 ± 13.92*
Poor (> 9) (n=12)	114.6 ± 6.3*
**P value*	*< 0.05*

Table 5: Relationship of Mean LVMI with Duration of Diabetes

Duration of DM (Years)	Mean LVMI (gm/m^2)
0 – 5 (n=20)	75.36 ± 9.53*
5.1 – 10 (n=20)	96.96 ± 13.76*
> 10 (n=9)	115.2 ± 13.39*
**P value*	*< 0.05*

(n=16), 10 (62.5%) cases had good glycemic control, 4 (25%) cases had fair glycemic control and only 2 (12.5%) cases had poor glycemic control. In group III (n=15), only 1 (6.66%) case had good glycemic control, 4 (26.66%) cases had fair glycemic control and 10 (66.66%) cases had poor glycemic control.

In group I (n=18), 15 (83.33%) cases had no retinopathy, 3 (16.66%) cases had pre-proliferative retinopathy. In group II (n=16), 7 (43.75%) cases had no retinopathy, 7 (43.75%) cases had pre-proliferative retinopathy and only 2 (12.5%) cases had proliferative type of retinopathy. In group III (n=15), 8(53.33%) cases had pre-proliferative retinopathy and 7 (46.66%) had proliferative retinopathy. None had a normal fundus.

In a group of patients with good glycemic control (n=28), 18 (64.28%) had no retinopathy, 9(34.14%) had pre proliferative retinopathy and only 1 (3.57%) had proliferative retinopathy. In patients with fair glycemic control (n=11), 3 (27.27%) had no retinopathy, 6 (54.54%) had pre proliferative retinopathy and remaining 2 (18.18%) had proliferative retinopathy. In patients with poor glycemic control (n=10), only 1 (10%) had no retinopathy, 3 (30%) had pre proliferative retinopathy and 6 (60%) had proliferative retinopathy.

In group of patients with duration of DM <5 years (n=20), 16 (80%) had no nephropathy, 4 (20%) had incipient nephropathy and no subject had overt nephropathy. In second group of patients with duration of DM between 5-10 years (n=20), only 2 (10%) had no nephropathy, 11 (55%) had incipient nephropathy and 7 (35%) had overt nephropathy. In third group of patients with duration of DM >10 years (n=9), 1 (11.11%) had incipient nephropathy and 8 (88.88%) had overt nephropathy.

Mean LVMI increased progressively with increase in proteinuria, duration of DM, poor glycemic control and worsening retinopathy. Increase in LVMI was due to increase in both SVTd and PWTd (SVTd> PWTd). Nephropathy and retinopathy worsened with the increase in duration of DM and poor glycemic control.

DISCUSSION

The relative mortality from cardiovascular disease is on average increased 40 fold in type I diabetic patients with nephropathy compared with general population (7). Increased left ventricular mass may contribute to the increased cardiovascular risk. Because left ventricular hypertrophy (LVH) is an ominous prognostic sign and an independent risk factor for sudden death, ventricular dysarrhythmia, myocardial ischemia, coronary artery disease and heart failure (8).

Patients with diabetic nephropathy have poorer metabolic control than patients with normoalbuminuria. Given that it reflects a persistently higher glucose level over several years this metabolic abnormality might contribute to the development of increased LVMI in type I DM patients with diabetic nephropathy (9). The present study showed direct association of increased proteinuria with increased LVMI.

Previous evidence of an association between, proteinuria and LVMI came form Sampson MJ et al (1990) (10), Sato A et al (1999) (11), Carugo S et al (2001) (12) who have reported direct association of increased proteinuria with increased LVMI; while a study conducted by Grenfell A et al (1988) (13) showed increased LMI with increased serum creatinine. The present study did not consider a parameter like serum creatinine for correlation with LVMI.

Literature says that increased LVMI is multifactorial and risk factors can be divided into two major categories, hemodynamic and non hemodynamic. The hemodynamic factors consists of blood pressure and volume overload. A volume overload might be induced in type I DM by exogenous insulin administration because of its documented acute effect on both peripheral resistance (14) and sodium retention (15). Alteration of myocardial substrate delivery to the mitochondria is impaired in diabetics which may lead to energy depleted state observed in heart failure (8).

LVH is known to be influenced by several non-hemodynamic factors that may also increase coronary risk. These included obesity and age (16), blood viscosity (17), salt intake (18) and insulin resistance. Sodium lithium erythrocyte counter transport is enhanced in diabetic nephropathy (19) and

association of this abnormality with LVH has been suggested (20).

Poor glycemic control, worsening retinopathy and increase duration of DM showed significant correlation with increased LVMI in the present study. Sato A et al (1998) (9) also reported significant correlation between glycemic control, duration of DM and severity of nephropathy and LVMI.

Thus the increased left ventricular mass index is a strong and independent risk factor for cardiovascular mortality over and above the extent of coronary artery disease.

The larger studies with more number of cases in Indian population are needed to confirm the results of present study.

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