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General Medicine

A STUDY OF RELATION OF HAEMOGLOBIN A1C TO LEFT VENTRICULAR DIASTOLIC FUNCTION IN PATIENTS WITH TYPE 1 DIABETES MELLITUS ON REGULAR TREATMENT WITHOUT OVERT HEART DISEASE

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ABSTRACT

Aims of the Study: To study about the echo cardio graphic findings in type -1 diabetic patients who are on regular treatment and study about glycaemic control, detect to early cardiac changes and prevent complications.

Material & Methods: The Clinical materials were of Type-1 Diabetes Mellitus individuals selected from Diabetic in the Tertiary Care Hospital. About 87 patients were subjected to initial assessment it included through clinical examination.

Results: The total study population included 50 patients were grouped into 2 categories, Patients with HbA1C >7, Patients with HbA1C < 7. Each group comprised of 25 patients each.

Conclusion: Asymptomatic diastolic dysfunction is common in patients with type 1 diabetes mellitus and can be picked up early before the clinical manifestation, Severity of the diastolic dysfunction correlates with the glycaemic control.

KEYWORDS : Haemoglobin, Left Ventricular Diastolic Function, Diabetew Mellitus

Introduction

Diabetes *mellitus* is a syndrome of chronic hyperglycaemia due to relative insulin deficiency, resistance, or both. It affects more than 120 million people world-wide, and it is estimated that it will affect 220 million by the year 2020.

Diabetes is usually irreversible and, although patients can have a reasonably normal lifestyle, its late complications result in reduced life expectancy and major health costs.

These include macro vascular disease, leading to an increased prevalence of coronary artery disease, peripheral vascular disease and stroke, and micro vascular damage causing diabetic retinopathy and nephropathy.

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, >360 million individuals will have diabetes by the year 2030.

Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly because of increasing obesity and reduced activity levels as countries become more industrialized.

Approximately 1.5 million individuals (>20 years) were newly diagnosed with diabetes in 2005. DM increases with ageing.

Type 1 diabetes is a disease resulting in insulin deficiency. In western countries almost all patients have the immune-mediated form of the disease (type 1A). Type 1 diabetes is prominent as a disease of childhood, reaching a peak incidence around the time of puberty, but can present at any age.

The Diabetes Control and Complications Trial (DCCT)[1] provided definitive proof that reduction in chronic hyperglycemia can prevent many of the early complications of type1 DM

In DCCT trial individuals in the intensive diabetes management group achieved a substantially lower hemoglobin A1C (7.3%) than individuals in the conventional diabetes management group (9.1%).

The DCCT demonstrated that improvement of glycaemic control reduced non proliferative and proliferative retinopathy (47% reduction), microalbuminuria (39% reduction), clinical nephropathy (54% reduction), and neuropathy (60% reduction). Improved glycaemic control also slowed the progression of early diabetic complications.

Diabetes mellitus (DM) is a risk factor for the development of symptomatic heart failure[2].Heart failure that occurs as the result of impaired myocardial relaxation and compliance has been termed diastolic heart failure[3]. Diastolic heart failure develops despite normal left ventricular systolic contractile function and leads to significant morbidity, medical costs, and mortality.[4]

There are few data on the appearance of markers of subclinical cardiovascular disease, which usually precede macrovascular disease in type 1 diabetes mellitus. Possible mechanisms for a specific diabetic cardiomyopathy include abnormalities of small intramural coronary vessels, deposition of collagen, and lipids and metabolic derangements that alter actomyosin and myosin adenosine triphosphatase activities[5].

Diastolic parameters are also highly influenced by changes in volume status, blood pressure, and heart rate, further complicating their interpretation in patients with diabetes. In addition, more exact analysis of left ventricular diastolic function requires direct left ventricular pressure measurements, which are not appropriate for clinical studies in healthy individuals. Noninvasive echocardiography with Doppler measurements of transmitral blood flow, together with other measurements, have become the preferred means to evaluate diastolic function noninvasively[6]. In this study, we sought to assess the occurrence of markers of subclinical cardiac (diastolic) dysfunction in asymptomatic patients with type 1 DM without any suggestion of macrovascular cardiac disease, and to evaluate the relation between diastolic dysfunction and glycemic control using echocardiographic techniques.

Aim of the Study

- To study about the echo cardio graphic findings in type -1 diabetic patients who are on regular treatment.
- To study about glycaemic control .
- To detect early cardiac changes and prevent complications

MATERIALS AND METHODS

The Clinical materials were of Type-1 Diabetes Mellitus individuals selected from Diabetic in the Tertiary Care Hospital.

About 87 patients were subjected to initial assessment it included through clinical examination, routine blood investigation consisting of complete blood count, biochemistry investigation, ECG , estimation of HbA1c and echo cardiography were done from which 50 patients were included in the study.

Statistical analysis

The Wilcoxon rank-sum test was used to analyze differences between the groups. Pearson's correlation analysis was used to measure the strength of association between pairs of variables. Simple and multiple linear regressions was used to assess the relation between diastolic indices and predictor variables (age, sex, HbA1c, duration of diabetes, nephropathy, and systolic blood pressure).

RESULTS

Clinical characteristics of patients with HbA1C >7 and HbA1C<7

CHARACTERISTIC	HbA1C <7	HbA1C>7
Age in years	28±10	28±9
Men	12	13
Body mass index(kg/m2)	22±6	24±5
Systolic blood pressure	110±9	110±11
Diastolic blood pressure	75±3	72±3
Heart rate(beats/min)	71±5	78±9

Other clinical characteristics of patients with HbA1C>7

Characteristics	HbA1C>7 (n=25)
Duration of diabetes	15±9
Mean HbA1C	7±1.5
Total serum cholesterol(mg/dl)	171±32
HDL(mg/dl)	53±18
LDL(mg/dl)	101±19
Triglycerides(mg/dl)	100±37

BASELINE ECHOCARDIOGRAPHIC CHARACTERISTICS OF ALL PATIENTS INCLUDED IN STUDY

CHARACTERISTIC	HbA1C <7 patients	HbA1C>7 Patients	p value
Left atrial area(cm2)	15.1±2.6	19±5.1	0.07
LV mass index(gm/m2)	91±36	106±40	0.06
LV ejection fraction(%)	65±4	66±5	0.2
Posterior LV thickness (cm)	0.7±0.1	0.91±0.3	0.001
Interventricular septal thickness(cm)	0.97±0.2	1±0.2	0.33
LV end diastolic diameter(cm)	4±0.3	4±0.4	0.61
LV end systolic diameter(cm)	2.3±0.4	2.4±0.6	0.73

DOPPLER INDICES IN PATIENTS WITH HbA1C>7 AND HbA1C <7

VARIABLE	HbA1C <7 (n=25)	HbA1C>7 (n = 25)	p value
LV peak early transmitral flow velocity E (cm/s)	75±1.1	77±0.9	0.3
Peak atrial contraction A (cm/s)	48±15	70±14	0.003
E/A ratio	1.6±0.3	1.28±0.31	0.01
Deceleration time (ms)	185±36	209±34	0.02
Isovolumic relaxation time (ms)	71±8	99±11	0.003

DISCUSSION

In this study, we found a higher prevalence of asymptomatic diastolic dysfunction in type 1 diabetes mellitus with HbA1c>7, in the absence of hypertension and cardiac disease.

These results support the concept of a specific Subclinical Diabetic Cardiomyopathy, which may be related to glycaemic control.

It showed that children and adolescents with type 1diabetes had altered cardiac function compared with age-matched individuals without diabetes.

Subjects included in the study had no cardiac signs or symptoms or diabetes complications, and were not taking medications known to modify cardiac structure or function.

The most striking findings were recorded in patients with type 1 diabetes, with HbA1C >7 who had reduced diastolic function compared with subjects with HbA1C<7.

Prolonged isovolumic relaxation time reflects the rate of active left ventricular diastolic relaxation between aortic valve closure and opening of the mitral valve. Relaxation of the myocardium is an energy dependent process requiring calcium sequestration from the cytosol into the sarcoplasmic reticulum, and it is altered in diabetes.

Interestingly, recent magnetic resonance studies have correlated changes in myocardial high-energy phosphates and parameters of diastolic function in patients with type 2 diabetes.

Experimental studies have also shown abnormalities in the calcium pump activity in diabetic animals (diamante et al (2003)[7]

In this study, we found low Trans mitral E/A ratio as an evidence of reduced diastolic function, left ventricular chamber compliance, and changes in the left atrial pressure. In the presence of mild diastolic dysfunction, early filling is often reduced, leading to an exaggerated atrial contribution to left ventricular filling and a low E/A ratio.

In more advanced heart failure, this pattern is often lost due to high left atrial and left ventricular pressure and the E/A ratio pseudo-normalizes or increases, complicating interpretation (Garcia et al (1998)[8]

Prior studies have shown a correlation between HbA1c and diastolic function in older individuals with type 1 diabetes, suggesting that glycaemic control maybe an important determinant of diastolic function - Shishehbor (2003)[9]

Hyperglycemia influences heart metabolism, the production of advanced glycosylation end products, oxidative stress, and protein kinase C activation.

The relation between glycaemic control and diastolic indexes in study supports the hypothesis that hyperglycemia by itself can lead to Subclinical Cardiomyopathy.

Results indicate that diabetic patients with worse glycaemic control are at an increased risk of early diastolic dysfunction.

Therefore, in our study, patients with type 1 diabetes with HbA1C>7 had increased isovolumic relaxation time, and a decreased E/A ratio compared with patients with HbA1C<7.

These results are consistent with prior studies in asymptomatic normotensive type 1 and 2 diabetic patients (Young LH (2004)[10], Zabalgoitia M (2001)[11] , Liu JE(2001)[12]; Shivalkar (2005) [13] Grand (2006)[14] Also, diastolic dysfunction was closely related to the duration of diabetes.

Further study is needed to determine whether

- Intensification of glycaemic control improves diastolic parameters
- Drugs that could interfere cellular level in cardiac metabolism
- Is diastolic dysfunction reversible ,if so, the time limit

Suysetal Utilized conventional Echocardiography / Doppler as well as tissue Doppler techniques and found abnormalities india stolic function in both girls and boys with type 1 diabetes. Both had prolonged isovolumic relaxation times, which reflect the rate of active left ventricular diastolic relaxation between aortic valve closure and the opening of the mitral valve.

Most novel in the study by Suys et al. were the tissue Doppler findings that myocardial relaxation velocity during early diastolic filling (E, sometimes termed Em) was reduced in girls, but not boys, with type 1 diabetes. Tissue Doppler tracks the left ventricular myocardium and provides information on diastolic function, making it less dependent on preload or volume status than traditional echo/Doppler techniques. The mean E velocities were lower in the diabetic girls, and a similar trend was observed for the more commonly measured maximal Evelocities. Somewhat surprisingly, there were no clear relationships between parameters of diastolic function and diabetes duration, BMI, or HbA1c.

Prior studies have shown a correlation between HbA1c and diastolic function in older individuals with type 1 diabetes, suggesting that Glycemic control may be an important determinant of diastolic function.

Patients with type 2 diabetes mellitus may develop subclinical LV dysfunction. The Strong Heart Study demonstrated impaired LV systolic function in type 2 diabetes mellitus with Doppler echocardiography. Fang et al found a high prevalence of subclinical LV systolic and diastolic dysfunction in patients with type 2 diabetes mellitus without ischemia or LV hypertrophy manifest as impaired systolic and diastolic myocardial velocities. When asymptomatic patients with type 2 diabetes mellitus were compared with age- and BMI-matched controls, patients with diabetes mellitus had impaired longitudinal, but preserved circumferential and radial systolic as well as diastolic function.

The study by von Bibra et al showed that intensive metabolic control with insulin therapy resulted in improvements in diastolic but not in systolic function, whereas studies by others failed to demonstrate improvements in either diastolic or systolic function, using tissue Doppler and ejection fraction measures, despite better glycemic control.

Dr Raghib Hasan, Dr M. Ghosh study has shown that HbA1c% measurement can be a very good indicator of long-term prognosis in diabetics. Even young diabetics with normal systolic ventricular function have diastolic dysfunction, which serves as a indicator of a diabetic cardiomyopathy. The results from this study reinforce the important role of Doppler echocardiography to evaluate the heart diastolic function parameters in diabetics.

SUMMARY

- Left ventricular diastolic dysfunction is a core feature of diabetic heart disease.
- The aim of this prospective study was to evaluate the relation of hemoglobin A1c and diastolic function in type 1diabetes mellitus. We examined echocardiographic studies of 25 patients with type 1 diabetes without clinical evidence of heart disease and hemoglobin A1C<7 and
- 25 patients with type 1 diabetes without clinical evidence of heart disease and hemoglobin A1C>7.
- In patients with type 1 diabetes without clinical evidence of heart disease and HbA1c >7, there was a diastolic dysfunction with lower trans mitral E/A ratio (1.28$\pm$0.3 vs 1.6$\pm$0.3 p=0.01), more prolonged isovolumic relaxation time (99±11 vs 71±8) in comparison with patients with type 1 diabetes without clinical evidence of heart disease and hemoglobin A1C<7 subjects.

CONCLUSION

HbA1c correlated with diastolic Doppler indices.

1. Asymptomatic diastolic dysfunction is common in patients with type 1 diabetes mellitus and can be picked up early before the clinical manifestation.
2. Severity of the diastolic dysfunction correlates with the glycaemic control.
3. Theoretical reversibility of these early cardiac changes with drugs can prevent progress in the clinical heart failure.

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