Glycosylated Hemoglobin (HbA1c) is a reliable Predictor of left ventricular hypertrophy (LVH) and left ventricular diastolic dysfunction (LVDD) in newly diagnosed type 2 diabetic patients of western Uttar Pradesh

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Abstract- Cardiovascular diseases like congestive heart failure, coronary artery disease, myocardial infarction account for highest mortality in diabetic patient. Left ventricular hypertrophy which is an ominous prognostic sign and independent risk factor for cardiac events is often present along with left ventricular diastolic dysfunction (LVDD) in type 2 diabetes mellitus patients. The aim of the present study is to verify whether HbA1c detect pre-clinical diastolic dysfunction in type-2 diabetic patients. Total 100 patients of newly diagnosed type 2 diabetes mellitus were selected for this cross sectional study. Patients of age between 30 to 60 yrs were selected for the study. HbA1C was estimated by Boronate affinity chromatography. Left ventricular hypertrophy was detected by measuring left ventricular mass index (LVMI) using Transthoracic Echocardiography, according to recommendation of American Society of Echocardiography (ASE). HbA1c is seems to be a reliable predictor of LVDD. Our Study demonstrated a very significant positive correlation between level of glycosylated hemoglobin (HbA1C) and frequency of LVH and LVDD in the newly diagnosed cases of type 2 diabetes mellitus. Similar correlation was also observed with FPG.

Index Terms- Glycocolated Hemoglobin Left ventricular dysfunction

I. INTRODUCTION

Diabetes mellitus is a worldwide health problem, afflicting millions in both developed and developing countries. Moreover, there is emerging evidence that a diabetes-related syndrome called Syndrome-X (characterized by truncal obesity, insulin resistance, diabetes, high blood pressure and premature coronary artery disease) is the most important cause for the rapidly increasing urban menace of coronary artery disease afflicting urban middle and upper classes. Cardiovascular diseases like congestive heart failure, coronary artery disease, myocardial infarction account for highest mortality in diabetic patient. Left ventricular hypertrophy which is an ominous prognostic sign and independent risk factor for cardiac events is often present along with left ventricular diastolic dysfunction (LVDD) in type 2 diabetes mellitus patients. The possible contribution of hyperinsulinemia and hyperglycemia to left ventricular mass have been suggested in normotensive diabetic patient. Echocardiography provides a reliable non invasive tool for detection of LVDD and left ventricular mass and has been proven more sensitive method for detection of left ventricular hypertrophy than other techniques. Left ventricular mass in diabetic patients may also increases with the HbA1C level. So a poor glycemic control is also associated with more chances of having left ventricular hypertrophy. Hence, the aim of the present study is to verify whether HbA1c detect pre-clinical diastolic dysfunction in type-2 diabetic patients.

II. METHODS

Study population

This was a cross sectional study conducted at the L.L.R.M. Medical College, Meerut during 2012–2013 . All patients with type 2 diabetes mellitus who are attending Medicine OPD, Endocrinology OPD, were included in the study who fulfilled the following inclusion criteria.( Age > 30 years & < 60 years , Patient who gave written informed consent, Mentally and physically fit up to a minimum level required to participate in study and patients with newly diagnosed type 2 diabetes mellitus (with in 1 month) according to WHO criteria and ADA recommendations for diabetes mellitus)

The Exclusion criteria were: those who were unable to provide informed consent, any substance abuse, mental illness or
medical condition that in the opinion of investigator would make it difficult to participate in intervention and a patient of known hypertension with or without treatment, ischemic heart disease, cardiomyopathy, valvular heart disease, heart failure, chronic pulmonary illness, severe anaemia, hemoglobinopathies.

**Investigations:**
Fasting and Post prandial Plasma glucose (FPG and PPPG) – HbA1C
Electrocardiography (ECG)
Plane Chest X-ray

2D Echocardiography: M-mode and pulsed Doppler Transthoracic Echocardiography according to recommendation of American Society of Echocardiography

Venous blood was collected after 8 hours of fasting, into two test tubes; with P vial for plasma glucose and with Ethylene Diamine Tetra Acetic Acid (EDTA) for HbA1c.

**HbA1C** was estimated by Boronate affinity chromatography (HPLC) which separates total glycosylated haemoglobin by binding to solid–phase dihydroxyborate using Nycocard immunoassay kit (USA).

**Table showing diagnostic criteria for IFG, IGT & diabetes mellitus**

<table>
<thead>
<tr>
<th></th>
<th>FBS (mg/dl)</th>
<th>2 hr Glucose (mg/dl)</th>
<th>HbA1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 100</td>
<td>&lt; 140</td>
<td>&lt; 6</td>
</tr>
<tr>
<td>IFG</td>
<td>≥100 &amp; &lt; 126</td>
<td>&lt; 140</td>
<td>6 – 6.4</td>
</tr>
<tr>
<td>IGT</td>
<td>&lt; 126</td>
<td>≥ 140</td>
<td>6- 6.4</td>
</tr>
<tr>
<td>DIABETES</td>
<td>≥126</td>
<td>≥ 200</td>
<td>≥ 6.5</td>
</tr>
</tbody>
</table>

**LEFT VENTRICULAR HYPERTROPHY**

Left ventricular hypertrophy was detected by measuring left ventricular mass index (LVM) using Transthoracic Echocardiography, according to recommendation of American Society of Echocardiography (ASE).

The following M Mode parameters were measured -

- Left ventricular end diastolic diameter (LVIDed)
- Left ventricular end systolic diameter (LVIDes)
- Ventricular septum thickness (IVSTed)
- Posterior wall thickness in diastole (PWTed)

**Left ventricular mass (LVM):** calculated by ASE formula i.e. LVM = 0.8[1.04{(LVIDed+PWTed+IVSTed³-(LVIDed³)}]+0.6 gm

Left ventricular mass index (LVMI)- LVM / BSA

LVH is considered if LVMI >45 g/m².7 in female and >49 g/m².7 in male.

**LEFT VENTRICULAR DIASTOLIC DYSFUNCTION:**

This was evaluated by Pulsed Doppler echocardiography. Pulsed-wave Doppler (PWD)-derived transmitral inflow velocities were obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips. Measurements included the transmitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities to calculate E/A ratio, isovolumetric relaxation time (IVRT) and deceleration time (DT). For tissue Doppler imaging (TDI), the mitral annulus velocity was obtained with a 2 mm sample volume lateral side and septal side of the mitral annulus. Diastolic dysfunction was labeled according to the standard guidelines. Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson’s method; and, LVEF ≥ 50% was considered as normal.

All echocardiographic measurements were averaged over three consecutive cardiac cycles, measured by a single investigator blinded to all other variables. LV diastolic dysfunction was considered to be present if any of the following findings were seen, as previously described:

- E/A ratio < 1 or > 2
- DT < 150 or > 220 ms,
- IVRT < 60 or > 100 ms, or
- E/e’ ratio > 15

Evaluation of different degrees of diastolic dysfunction using data obtained from the transmital flow pattern (top) and analysis of tissue Doppler at the mitral annulus level (bottom). Legend: DD-diastolic dysfunction; DDT-diastolic deceleration time; Transmitral flow velocity during early ventricular filling; A-transmitral flow velocity during atrial contraction; e’-Tissue Dopper velocity at the mitral annulus level during early ventricular filling.
2D-ECHO PHOTOGRAPHS SHOWING LVDD
Statistical analysis: Data were analysed for mean, percentage, standard deviation, Student’s t’ test, Fisher’s exact test, by using SPSS-16 (Statistical Package for the Social Sciences) for Windows (SPSS, Chicago, IL). The t’-test and Fisher’s exact tests were applied to study quantitative and qualitative data, respectively with P-value < 0.05 was considered statistically significant.

III. OBSERVATIONS AND RESULTS

Table 2: Age and Sex wise distribution of cases

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Male</th>
<th></th>
<th>Female</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>30-40</td>
<td>04</td>
<td>04</td>
<td>04</td>
<td>04</td>
<td>08</td>
<td>08</td>
</tr>
<tr>
<td>41-50</td>
<td>16</td>
<td>16</td>
<td>20</td>
<td>20</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>51-60</td>
<td>40</td>
<td>40</td>
<td>16</td>
<td>16</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>60</td>
<td>40</td>
<td>40</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Total 100 patients of newly diagnosed type 2 diabetes mellitus were selected for this cross sectional study. Out of which 60 (60%) were males and 40 (40%) females. Patients of age between 30 to 60 yrs were selected for the study. Maximum patient belongs to age group 50-60 yrs (56 patients) and minimum in age group 30-40 yrs (08 patients).
Table 3: Frequency of Left Ventricular hypertrophy in Subjects and gender wise distribution of cases

<table>
<thead>
<tr>
<th>Mild LVH</th>
<th>Moderate LVH</th>
<th>Severe LVH</th>
<th>Overall cases of LVH</th>
<th>Mild LVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>27</td>
<td>0</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td>Female</td>
<td>09</td>
<td>0</td>
<td>0</td>
<td>09</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>0</td>
<td>0</td>
<td>36</td>
</tr>
</tbody>
</table>

Table 3 shows that, out of 100 patients of newly diagnosed normotensive type 2 DM; 36% patients were found to have left ventricular hypertrophy. Only mild left ventricular hypertrophy was present in all cases as detected by 2D echocardiography by measuring left ventricular mass index. Out of 36 cases, 27 were male and 09 were females.

Figure 2: Frequency of Left Ventricular hypertrophy in subjects and gender wise distribution of cases
Table-4: Comparative Parameters of the Patients with LV Diastolic dysfunction

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>WITH LVDD</th>
<th>WITHOUT LVDD</th>
<th>P VALUE (‘t’ test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>42</td>
<td>58</td>
<td>n/a</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>192.05 ±29.82</td>
<td>173.67 ± 27.71</td>
<td>0.0020</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>7.69 ±1.01</td>
<td>7.26 ± 0.74</td>
<td>0.0157</td>
</tr>
<tr>
<td>Age ( year)</td>
<td>54.56 ± 6.49</td>
<td>46.48 ±7.15</td>
<td>0.0012</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.09±2.84</td>
<td>25.15±2.36</td>
<td>0.0743</td>
</tr>
</tbody>
</table>

Mean FPG of subjects with LVDD was 192.05 ±29.82/dl and that of population without LVDD was 173.67 ± 27.71mg/dl .This shows that FPG is positively associated with the incidence of LVDD in population as mean of FPG of population with LVDD was higher as compare to population without LVDD and correlation was found very significant (p=0.0020).

The mean HbA1C of subjects with LVDD was 7.69 ± 1.01 as compare to subjects without LVDD 7.26 ± 0.74 the Correlation was found significant using unpaired t test (p value 0.0157).This signifies that higher the value of HbA1C at the time of diagnosis, higher will be the incidence of LVDD .Mean age of subjects with LVDD was 54.56 ± 6.49yrs and that of population without LVDD was 46.48 ± 7.15yrs. Age is positively associated with the incidence of diabetic LVDD in population as mean of age of population with LVDD was higher as compare to population without LVDD and correlation was found very significant (p=0.0012) mean body mass index of subjects with LVDD was 26.09±2.84 kg/m² and that of population without LVDD was 25.15±2.36kg/m² .BMI is not positively associated with the incidence of diabetic LVDD in population as mean of BMI of population and correlation was not significant (p=0.0743).

IV. DISCUSSION

Diabetes Mellitus is a metabolic disease, associated with a number of complications including nephropathy, neuropathy, ischemic heart disease, cerebrovascular disease and peripheral vascular diseases. Type 2 DM is likely to remain undiagnosed for years. The gap between the onset of the disease and clinical diagnosis of diabetes leads to the development of these chronic complications, which are the leading causes of premature mortality among diabetic patients. In this study, which is one of the first studies in this regards in western U.P., we assessed the correlation of left ventricular diastolic dysfunction (LVDD) with various parameters like glycosylated haemoglobin (HbA1C), plasma Glucose, Age and body mass index (BMI). In our study, incidence of left ventricular hypertrophy in Type 2 diabetics without known hypertension, cardiac, cerebrovascular or peripheral vascular disease, has demonstrated that LVH (defined according to the ASE guidelines) was common, occurring among 36 % of the patients, which is similar to study done by Somratne et al suggesting that type 2 diabetes per se is associated with LVH. Left ventricular hypertrophy which is an ominous prognostic sign and independent risk factor for cardiac events is often present in type 2 diabetes mellitus patients. The possible contribution of hyperinsulinemia and hyperglycemia to left ventricular mass has been suggested in normotensive diabetic patient but. Dawson et al in UK found a very high prevalence of 74 % which may be because he included already diagnosed cases of type 2 DM. In this study a positive correlation was found between prevalence of LVH and level of HbA1C and Age but association with BMI was not significant. Incidence of LVH was found higher in males as compare to
females. Study demonstrates high incidence of diastolic dysfunction in normotensive and asymptomatic type 2 diabetics even at the time of diagnosis and this finding has a positive correlation with HbA1C and age at the time of diagnosis of diabetes. No significant HbA1C and age at the time of diagnosis of diabetes.

V. CONCLUSION

HbA1c is seems to be reliable predictor of LVDD. Our Study demonstrated a very significant positive correlation between level of glycosylated hemoglobin(HbA1C) and frequency of LVH and LVDD in the newly diagnosed cases of type 2 diabetes mellitus. Similar correlation was also observed with FPG.

REFERENCES


AUTHORS

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