Cardio Vascular Risk Assessment in Type 2 Diabetes Mellitus - A Pilot Study

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Abstract: The World Health Organization has described that diabetes has reached epidemic proportions, as number of diabetics / prevalence has gone up dramatically over last few decades, and estimates that by current trend by 2025 the number of diabetics will be more than 300 million. The rise in type 2 diabetes is occurring much faster than type 1, because of increasing obesity and sedentary lifestyle. A recent study conducted in six different cities in India states that prevalence rate is much higher and in Bangalore it is 12.4%. When patients with diabetes develop clinical cardiovascular disease, they sustain a worse prognosis for survival than do cardiovascular disease patients without diabetes. Available data indicates that type 2 diabetics are prone to inflammation and thereby CVD. This provides scope for exploring the same in prevention / management of inflammatory markers, and help to prevent the CVD risk in type 2 diabetics. Hence this study was undertaken to evaluate the status of inflammatory markers in type 2 diabetes mellitus viz. C - reactive protein, lipoprotein (a), homocysteine. This is a case control study, where type 2 diabetes mellitus subjects were included and categorized into two groups, 50 each, namely, newly detected (NDM) and more than 5yrs (DM5). These groups were compared with 50 control (CNT) subjects. These subjects were analyzed for their anthropometric measurements to mark the obesity grades and biochemical estimations namely fasting blood sugar, lipid profile and estimation of biomarkers homocysteine (Hcy), C - reactive protein (CRP), lipoprotein (a) Lp(a), vitamin B₁₂ (B12).

1. Introduction

The impact of diabetes on the incidence of CVD is high when compared to the non-diabetes. It is possible that precursors of CVD have a greater effect in those with diabetes than in non-diabetic individuals [1]. According to WHO, the estimated diabetic patients in India are more than 20million, which is estimated to reach 55million by 2025. Studies have shown that there is an average annual increase in rate of heart disease from 7 per 1,000 to 68 per 1,000 [2]. Despite earlier treatment, there is a continued incidence of CVD, in people with T2DM.

In 1970's the prevalence of diabetes was approximately 2% among urban population in India, but at present the prevalence is more than 12%. A recent study conducted in six different cities; support that prevalence rate is much higher in metropolitan cities – Hyderabad (16.6%), Chennai (13.5%), Bangalore (12.4%), Kolkata (11.7%), Delhi (11.6%), Mumbai (9.3%) [3].

The so called “Asian Indian Phenotype” refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity that is higher waist circumference despite lower body mass index, lower adiponectin and higher sensitivity C-reactive protein levels [4].
2. Relationship between type 2 diabetes and cardiovascular disease

The relationship between diabetes and CVD is complex and multifactorial. Atherosclerosis is the major threat to microvasculature in diabetes. Dyslipidemia is highly correlated with atherosclerosis, and up to 97% of patients with diabetes are dyslipidemic. In addition to the characteristic pattern of increased triglycerides and decreased HDL cholesterol found in the plasma of patients with diabetes, abnormalities are seen in the structure of the lipoprotein particles[5]. Healthy endothelium regulates blood vessel tone, platelet activation, leukocyte adhesion, thrombogenesis, and inflammation. The net effect of healthy endothelium is vasodilatory, anti-atherogenic, and anti-inflammatory. When these mechanisms are defective, the process of atherosclerosis is accelerated [6]. Therefore, both insulin deficiency and insulin resistance promote dyslipidemia [7].

Inflammation is a normal response to tissue injury or pathogen exposure and is a critical factor in the body’s ability to heal itself or to fight off infection. The inflammatory response involves the part, by a family of cytokines and chemokines [8]. Although inflammation is beneficial, if this response is chronically activated it can have a detrimental effect.

Diabetes has long been considered a state of evidence to suggest that this immune activation may precede insulin resistance in diabetic and prediabetic states and ultimately may be the factor that initially increases in these disease processes [9]. The concept of inflammation participates in all phases of atherosclerosis, from initiation through progression and including clinical complications. The clinical application of this basic science has led to investigations of bio-markers of inflammation as additions to the traditional, well validated risk factors in cardiovascular event prediction [10].

Bio-markers of inflammation have a number of applications in cardiovascular fields: prediction of first ever cardiovascular event, determination of prognosis in those with established disease, providing a target of therapy / serving to guide therapy through proper food choices [11]. For this purpose C - reactive protein, lipoprotein (a), homocysteine are a few serum analysis tools that can be used to predict the cardiovascular risk [12-13].

Elevated homocysteine levels can be caused by varied factors, including folate and B-vitamins deficiency, pre-existing atherosclerotic disease, diabetes and reaction of various drugs [13]. A study conducted by Kilmer McCully concluded, that the severely elevated levels of homocysteine were directly responsible for the various vascular lesions in these individuals and he further postulated that moderately elevated levels of homocysteine due to heterozygous mutations in homocysteine related genes or poor vitamin status would also lead to increased risk of cardiovascular disease [14]. Ueland, et al., showed that the combined effects of elevated homocysteine levels increased the risk of total mortality in 587 diabetes mellitus patients who had been diagnostically confirmed for coronary artery disease. The investigators concluded that the combination of elevated homocysteine and diabetes exponentially increased the risk of mortality in diabetic patients [15].

The link between heart disease and diabetes is inflammation. and for many patients that inflammation, this is because fat cells or “adipocytes”, which produces a messenger proteins that turn on the production of CRP [16]. Researchers from Reykjavik study indicated that CRP may be only a moderate risk factor for cardiovascular disease [17], Jupiter trial studies have found elevated CRP levels with hyperlipidemia [18]. In a meta-analysis of 20 studies involving 1,466 patients with coronary artery disease, CRP levels were found to be high. The levels were reduced with regular exercise interventions [19]. Further to confirm CRP as a bystander or active participant in atherogenesis, a 2008 study compared people with various genetic CRP variants, which showed that those with high CRP due to genetic variation had increased risk of cardiovascular disease compared to those with a normal or low CRP [20].

Lp(a) indicates a coagulant risk of plaque thrombosis [21]. Apo(a) contains domains that are very similar to plasminogen (PLG) [22]. Lp(a) accumulates in the vessel wall and inhibits binding of PLG to the cell surface, reducing plasmin generation which increases clotting. This inhibition of PLG by Lp(a) also promotes proliferation of smooth muscle cells. These unique features of Lp(a) suggest Lp(a) causes generation of clots and atherosclerosis [23]. Also, type 2 diabetes mellitus has a strong genetic component of dyslipidemia which serve as a common basis for CVD risk [24]. Numerous studies show a strong correlation between elevated Lp(a) and CVD, has led to a conclusion that Lp(a) is an important, independent predictor of cardiovascular disease [25]. Several animal studies have shown that Lp(a) may directly contribute to atherosclerotic damage by increasing plaque size, inflammation, instability, and smooth muscle cell growth. Genetic data also support the theory that Lp(a) causes cardiovascular disease [26].
In view of the consequences associated with T2DM and increased number of diabetics in India, there is a need for data on inflammatory markers, to plan prevention and management of CVD among diabetics. Lack of data in this regard has prompted us to investigate the status of the selected inflammatory markers in relation to the duration of diabetes, which is a first study reporting such data among Indian subjects.

3. Materials & Methods

A case control study was undertaken in the year 2013 for a period of 6 months to analyze the inflammatory markers among newly detected (NDM) and known diabetic (DM5) subjects. There was a comparison between control subjects, newly detected and known type 2 diabetes mellitus.

Study sample: 50 subjects from different sectors were recruited for the study from the diabetic clinic. Before the initiation of the study, ethical clearance (IHEC-UOM No.89 Ph.D / 2013-14) was taken from the heads of the ethical committee of the institution. Permission was sought from the heads of the clinic, to recruit the subjects, for the study. The objective of the study was informed to the subjects who visited the hospital and subjects who volunteered to take part in the study were given the consent form.

The inclusion criterion was framed for the selection of subjects and those who met these criteria were selected for the study. The selection criteria was as follows: only subjects with type 2 diabetes mellitus in the age group of 30 to 70 yrs, both male and female, newly detected subjects (within a year) and subjects with diabetes mellitus for > 5 years, that is known diabetics were included. Subjects without any other co-morbidities/metabolic disorder and who agreed to participate and provide their consent to share all the required details for the study were selected.

The subjects were assessed for their anthropometric measurements; BMI was derived and compared with the ICMR ranges for obesity grades, their waist to hip ratio was calculated to arrive at central obesity values.

Blood sample (5 ml) was drawn from each subject after an overnight fast. After collection procedure few drops of blood was taken for estimation of peripheral blood smear and haemoglobin. Later the blood sample was centrifuged at 3500rpm for 10 -15min at room temperature to separate the serum for further analysis. After this procedure, the serum was analyzed for glucose, triglycerides, total cholesterol, homocysteine, C - reactive protein lipoprotein (a), vitamin B12. Hcy was estimated by enzymatic assay method, CRP by a latex – enhanced turbidimetric invito immune assay, Lp(a) by turbilatex and vitamin B12 by immunoassay method [26-27].

Statistical analysis: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation between study variables is done to find the correlation [28-29].

4. Result

Among the 50 subjects in NDM, 33 of them were males and 17 females. In the DM5 group, 30 were males and 20 were females. The age group of the subjects was 30-60yrs.

The somatic data is represented in Table 1. The BMI of the subjects was calculated and graded for obesity on the grounds of ICMR guidelines [30]. 96% of the NDM subjects had BMI levels of 18-23kg/m² and 74% of the DM5 subjects were found in this group. Waist to hip ratio, which marks the central obesity, was also calculated. 94% of the subjects from the NDM and 70% of the subjects from the DM5 were found in the range of 0.8-0.9 with a mean SD of 0.82 ±0.04.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Newly detected type 2 DM</th>
<th>Known type 2 DM - &gt;5yrs</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>44.52±10.60</td>
<td>42.46±8.86</td>
<td>58.14±10.87</td>
<td>48.37±12.26</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

Table 1: Somatic Status of the Subjects in Three Groups
The bio chemical analysis of the subjects is represented in table no.2. The Haemoglobin of all the subjects in both the groups was normal, but certain changes were found in the peripheral blood smear. Among the total number of subjects 5.3% had macrocytic anaemia, and in 1% dimorphic anaemia was found.

In glucose estimation among the NDM, 4% of the subjects were in the range of <100mg/dl, 48% of them between 100-126mg/dl and >126mg/dl respectively with a mean SD of 173.96±83.58. Among the DM5 8%, 58% and 34% were in the ranges <100mg/dl, 100-126mg/dl and >126mg/dl respectively with a mean SD of 177.80 ± 90.27.

Data related to the lipid profile was classified according to NCEP (national cholesterol education program) (Adult treatment panel III), guidelines[31], showed a distinctive atherogenic profile in majority of the subjects. 68% and 54% of the NDM and DM5 had a higher cholesterol levels. 84% and 76% of the NDM and DM5 had high triglyceride levels. These levels are higher than the desirable levels in the NCEP. It was observed that both mean total cholesterol and triglyceride levels were higher than the desirable level at least in 60% of the subjects.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Newly detected type 2 DM</th>
<th>Known type 2 DM - &gt;5yrs</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin %</td>
<td>14.16±2.17</td>
<td>14.25±1.86</td>
<td>13.78±1.98</td>
<td>14.06±2.00</td>
<td>0.465</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>86.28±11.1</td>
<td>173.96±83.58</td>
<td>177.86±90.27</td>
<td>146.03±82.57</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>191.60±61.93</td>
<td>184.18±35.33</td>
<td>194.54±47.81</td>
<td>190.11±49.42</td>
<td>0.561</td>
</tr>
<tr>
<td>TGL (mg/dl)</td>
<td>172.14±73.95</td>
<td>223.92±75.38</td>
<td>223.00±101.44</td>
<td>206.35±87.41</td>
<td>0.003**</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>42.50±4.32</td>
<td>44.46±5.69</td>
<td>45.26±4.33</td>
<td>44.07±4.93</td>
<td>0.015*</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>96.84±42.1</td>
<td>96.40±38.30</td>
<td>106.48±41.36</td>
<td>99.91±40.61</td>
<td>0.376</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>32.28±12.9</td>
<td>43.56±14.15</td>
<td>41.40±16.3</td>
<td>39.08±15.23</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

The graphical representation of the biomarkers is depicted in figure 1 – The normal levels of Hcy being 12-13μmol/L. It was found that 86% of the DM5 and 76% NDM were in the high normal range. The acceptable range for CRP is 3-10mg/l, it was seen that 24% of the DM5 were towards the higher levels and 6% of the NDM in that range. In Lp(a) , there was a remarkable difference in the two groups , the normal range being, 30mg/dl, 96% of the DM5 and 36% of the NDM are towards the high normal value. The vitamin B_{12} levels of both the groups was not influenced by the disease and values were all within the normal range, 211-911pg/ml.
Table 3: Comparison Of Homocystiene, C - reactive protein, Lipoprotein (A) And Vitamin B₁₂ in Vegetarian & Non-Vegetarian In Three Groups Of Patients Studied.

<table>
<thead>
<tr>
<th>Variables</th>
<th>VEG</th>
<th>NON-VEG</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Homocysteine</td>
<td>11.17±1.96</td>
<td>12.39±2.60</td>
<td>0.143</td>
</tr>
<tr>
<td>• CRP</td>
<td>3.55±0.33</td>
<td>3.68±0.39</td>
<td>0.294</td>
</tr>
<tr>
<td>• LP(a)</td>
<td>9.76±8.69</td>
<td>7.75±4.57</td>
<td>0.298</td>
</tr>
<tr>
<td>• Vit B₁₂</td>
<td>390.2±245.4</td>
<td>250.00±77.10</td>
<td>0.003**</td>
</tr>
<tr>
<td><strong>Newly detected type 2 DM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Homocysteine</td>
<td>27.39±19.82</td>
<td>20.65±7.66</td>
<td>0.090+</td>
</tr>
<tr>
<td>• CRP</td>
<td>3.53±0.53</td>
<td>4.74±2.61</td>
<td>0.153</td>
</tr>
<tr>
<td>• LP(a)</td>
<td>15.15±14.45</td>
<td>13.63±13.88</td>
<td>0.759</td>
</tr>
<tr>
<td>• Vit B₁₂</td>
<td>266.40±64.97</td>
<td>314.75±167.74</td>
<td>0.379</td>
</tr>
<tr>
<td><strong>Known type 2 DM &gt;5yrs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Homocysteine</td>
<td>22.59±5.69</td>
<td>21.37±6.39</td>
<td>0.506</td>
</tr>
<tr>
<td>• CRP</td>
<td>3.83±0.45</td>
<td>4.13±0.85</td>
<td>0.176</td>
</tr>
<tr>
<td>• LP(a)</td>
<td>23.31±10.23</td>
<td>32.70±13.75</td>
<td>0.015*</td>
</tr>
<tr>
<td>• Vit B₁₂</td>
<td>374.22±195.87</td>
<td>323.28±149.81</td>
<td>0.307</td>
</tr>
</tbody>
</table>

The grouping has been done on the dietary habits mainly - vegetarian and non-vegetarian, to note the differences between the two groups in the inflammatory biomarkers. The Hcy levels of NDM among vegetarians and non-vegetarians was 27.39±19.82 and 20.65±7.66 with a P value of 0.090+, and in DM5 it was 22.59±5.69 and 21.37±6.39. CRP values among the NDM in...
vegetarians and non-vegetarians was 3.53±0.53 and 4.74±2.61, among the DM5 it was, 3.83±0.45 and 4.13±0.85 respectively. Lp(a) values among the vegetarians and non-vegetarians in NDM was 15.15±14.45 and 13.63±13.88, among the DM5 it was 23.31±10.23 and 32.70±13.75 respectively. Vitamin B12 among the NDM in vegetarian and non-vegetarian was 266.40±64.97 and 314.75±167.74, and among the DM5 it was 374.22±195.87 and 323.28±149.81 respectively.

These values of these biomarkers were compared with at risk values to arrive at risk assessment in these subjects. The table no 4 gives the risk assessment of CVD in the two groups. 78% and 24% of the NDM and DM5 had high Lp(a) levels. CRP levels of 43% and 48% of the DM5 were high. Hcy levels of 76% of the NDM and 86% of the DM5 were found to be high. HDL of 90% of the NDM was high and 88% of the DM5 was high. LDL levels of 16% and 22% of the NDM and DM5 were high. TG of 42% of the NDM and 76% of the DM5 were high, all values exhibiting that were at risk for developing CVD.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>At risk values</th>
<th>Newly detected DM(n=50)</th>
<th>Known &gt;5yrs(n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lp(a) (mg/dl)</td>
<td>&lt;15-20</td>
<td>39(78.0%)</td>
<td>12(24.0%)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>CRP (lu/ml)</td>
<td>&gt;3</td>
<td>43(86.0%)</td>
<td>48(96.0%)</td>
<td>0.080+</td>
</tr>
<tr>
<td>Hcy (µmol/l)</td>
<td>&gt;15.0</td>
<td>38(76.0%)</td>
<td>43(86.0%)</td>
<td>0.202</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>&lt;50</td>
<td>45(90.0%)</td>
<td>44(88.0%)</td>
<td>0.749</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>&gt;130</td>
<td>8(16.0%)</td>
<td>11(22.0%)</td>
<td>0.444</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>&gt;150</td>
<td>42(84.0%)</td>
<td>38(76.0%)</td>
<td>0.317</td>
</tr>
</tbody>
</table>

5. Discussion

The present study was undertaken to mark the importance of bio markers in identifying the risk of cardio vascular disease in T2DM subjects and also to show, as the disease progresses the risk of CVD increases. For this purpose inflammatory bio-markers, Hcy, CRP, Lp (a) and Vit B\textsubscript{12} were compared with two groups NDM and DM5.

A large number of subjects selected for the study had a family history of diabetes, stating that diabetes is heredity. In most of the NDM, diabetes was found when they approached for a general check up and a few of them experienced symptoms of diabetes and had approached for analysis.

Anthropometric measurements height and weight were recorded to mark the obesity grades and WHR to mark the central obesity. The BMI results were compared with the ICMR classification and a large number of subjects were either obese or overweight. Subjects from both the groups had a higher value of WHR, which is they had central obesity which suggests that they did not follow a balanced diet and had a lack of exercise and improper lifestyle habits.

Subjects had normal haemoglobin levels in the range 12-16%. The peripheral blood smear which is an improvised test to know the haemoglobin condition among the diabetics was also done to know the type of anaemia. The results indicated normal haemoglobin among majority of the subjects.

It is a known fact that all the diabetics have high sugar levels, and as expected all the subjects selected have high glucose levels irrespective of the duration of the disease.

The lipid parameters namely cholesterol, triglycerides, HDL, LDL and VLDL were compared between the groups with the NCEP risk factor. These results showed varied changes in lipid profile. Most of the subjects had high cholesterol and LDL levels, which gives an impression that the diabetic subjects should follow a healthy diet containing more of good fats like monounsaturated and poly unsaturated fats, which in turn would help them from keeping their lipid levels normal, which is important for all diabetics.

Inflammation always proceeds with diabetes [34] and inflammatory bio – markers have always been linked with endothelial dysfunction in cardiovascular diseases. The estimation of the biomarkers – Hcy, CRP, Lp (a) and Vit B\textsubscript{12} helps in identifying the underlying problems of inflammation pertaining to heart and thereby reduces the complications of CVD in diabetic
people [35]. The levels of the biomarkers have been compared with the standards [36-38] and also with controls. Hcy levels of all the subjects were found to be in the high normal range and also when compared with the CVD risk assessment value, the levels of Hcy levels were found to be high. A study conducted by Minna Soinio and colleagues also arrived at a conclusion that high homocysteine can act as an independent marker for CVD risk [39]. Similarly elevated levels of CRP were found among the subjects from both the groups. When these levels were compared with the at risk value for CVD, the same result was obtained. Thus CRP also acts as an effective biomarker in identifying the underlying problems of inflammation. A study conducted by Masatsugu Horiuchi and Masaki Mogi Elevated also revealed similar result as follows - CRP is also a risk factor for the development of cardiovascular disease, irrespective of metabolic syndrome, mainly because of exaggeration of inflammation and oxidative stress. Given that CRP is a critical determinant of the exaggeration of cardiovascular disorders, including hypertension and metabolic disorders, not merely as a simple biomarker of these disease states, it is important to further examine the details of the signalling mechanism of CRP-mediated inflammation and oxidative stress and specific target organs of CRP and the localization of CRP receptors to understand the roles of CRP in the pathogenesis of metabolic syndrome and cardiovascular disease and to develop clinical interventions against CRP-mediated effects [40]. Lp(a) levels also were high normal among all the subjects from both the groups and also showed high levels when compared with at risk levels for CVD. It was also shown from the study that the Lp(a) levels were influenced from the lipid levels of the subjects. Numerous studies also have shown a strong correlation between elevated Lp(a) and CVD, has led to a conclusion that Lp(a) is an important, independent predictor of cardiovascular disease [41].

The European Atherosclerosis Society currently recommends that patients with diabetes should have their Lp(a) and other markers analysed and a higher level of these biomarkers and Lp(a) shows that- they are at risk for cardiovascular disease [42].

The Vit B12 levels of all the subjects from the groups were all within normal limits, but were higher among the DM5 subjects, but were within the normal levels. Several studies have found a deficiency of Vit B12 levels due to drug reaction metformin.

The study result thus establishes that there is a relationship between the levels of the markers and initiation of inflammation and with disease progression when compared between healthy controls, NDM and DM5. The Hcy levels gives a picture that there is an onset of inflammation once impairment in the insulin levels is found. CRP levels which is released by the liver in response to any inflammation in the body also depicts the same. Lp(a) levels is an independent marker and also predicts the lipid profile of the subjects. The vitamin B 12 levels of both the groups are not influenced by the disease as it is all within the normal range.

When the significance is compared between the three Lp(a) vs VitB12 shows a greater significance than the others Hcy vs VitB12, Hcy vs CRP. Hcy vs Lp(a) and CRP vs Lp(a) are also significant. When the same results are grouped according to food habits, among KD5 Lp(a) shows significant results when compared to others. The other results indicate a suggestive significance.

In conclusion, our finding state that Hcy, CRP, Lp(a) are all good markers for the detection of CVD risk among the T2Dm subjects. It also suggests that there is an increased risk in the same group as there is a progression in the disease and control of insulin levels and cholesterol levels play an important role. Also the risk can be reduced by modifications in the diet and bringing in lifestyle modifications and controlling the levels of these markers, thus reducing the risk of CVD in the group. Further studies in the same field in a larger group would provide an exact indicative range in the Indian population to assess such risk factors, as such studies are very scanty.

6. References


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[40] Masaki Mogi.,2011; C-Reactive Protein Beyond Biomarker of Inflammation in Metabolic Syndrome., Hypertension,57:672-673,, Department of Molecular Cardiovascular Biology and Pharmacology, Ehime University, Graduate School of Medicine, Shitsukawa, Tohon, Ehime 791-0295, Japan. E-mail horiuchi@m.ehime-u.ac.jp.
