Correlations between dyslipidemia and cardiovascular disease in patients of type 2 diabetes mellitus

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Abstract
Hyperlipidemia in association with insulin resistance is common in patients with type 2 diabetes mellitus. Insulin resistance and the ensuing hyperinsulinemia are associated with hypertriglyceridemia and low serum high-density lipoprotein (HDL) cholesterol concentrations. The lipoprotein abnormalities are related to the severity of the insulin resistance. The venous blood was collected for both fasting and post prandial for blood sugar estimation. The fasting blood samples were collected for the estimation of serum Total cholesterol, serum Triglycerides and serum HDL cholesterol estimation. In this study it was found that though the patients were on oral hypoglycaemic drugs and some patients were on Insulin the fasting blood sugar and post prandial blood sugar are significantly high in study groups when compared to control groups (P< 0.001).

Keywords: Correlations, dyslipidemia, cardiovascular disease

Introduction
Diabetes is well recognized as an independent risk factor for cardiovascular disease (CVD) in men and women. CVD is up to four times more common in people with diabetes than in those without, and 50 percent of diabetic people have evidence of CVD at the time of diagnosis [1]. Post infarction mortality is significantly higher in people with diabetes than in those without. It is estimated that 75 to 80 percent of diabetes related deaths are attributable to the macrovascular complications of the disease primarily cardiovascular disease, cerebrovascular disease, and peripheral vascular disease.
Atherosclerotic macro vascular complications occur at an earlier age and with greater severity in people with diabetes, and its pathogenesis is directly influenced by the diabetic state.
Long term exposure to elevated glucose levels can contribute to the endothelial dysfunction observed in diabetes. Increasing evidence suggest that endothelial dysfunction may play a central role in the development of atherosclerosis. Endothelial dysfunction is characterized by inhibited vasodilatation, increased proliferation of vascular smooth muscle, increased thrombogenesis, and proatherogenic cellular processes [2]. The accelerated atherosclerosis, endothelial dysfunction has been linked with increased thrombosis, hypertension, and dyslipidemia, all of which contribute to the pathogenesis of vascular disease in diabetes.
The dyslipidaemia is a condition marked by abnormal concentration of lipids or lipoproteins in blood, the typical atherogenic dyslipidemia includes increased plasma triglyceride levels as well as reduced HDL Cholesterol concentration and the presence of small, dense LDL cholesterol particles. The prevalence of dyslipidemia varies with the population being studied. The incidence is highest in patients with premature coronary heart disease (CHD), which can be defined as occurring before 55 to 60 years of age in men and before 65 years in women. In this setting, the prevalence of dyslipidemia is as high as 75 to 85 percent compared to approximately 40 to 48 percent in age-matched controls without CHD [3]. Hyperlipidemia in association with insulin resistance is common in patients with type 2 diabetes mellitus. Insulin resistance and the ensuing hyperinsulinemia are associated with hypertriglyceridemia and low serum high-density lipoprotein (HDL) cholesterol concentrations.
The lipoprotein abnormalities are related to the severity of the insulin resistance. A study that measured insulin sensitivity using a euglycemic clamp in patients with and without type 2 diabetes mellitus found that greater insulin resistance was associated with large very low density lipoprotein (VLDL) particle size, small low density lipoprotein (LDL) particle size, and small HDL particle size. Additionally, the number of VLDL, intermediate density lipoprotein (IDL), and LDL particles increased with increasing insulin resistance. Hypertriglyceridemia results both from increased substrate availability (glucose and free fatty acids) and from decreased lipolysis of VLDL triglyceride. According to the centers for disease control and prevention (CDC), 97% of adults with diabetes have one or more lipid abnormalities. The central characteristic of dyslipidemia in type 2 diabetes is an elevated triglyceride level, particularly triglyceride rich VLDL levels and decreased HDL cholesterol levels. The concentration of LDL cholesterol is usually not significantly different from that seen in non diabetic individuals [4, 5]. The type 2 diabetes typically have a preponderance of small, dense, oxidized LDL particles, which may increase atherogeneity, even if the absolute concentration of LDL cholesterol is not elevated [6].

Methodology
The patients for this study were selected according to the following criteria.

Inclusion criteria
1. Age more than 40 years
2. Type 2 Diabetes Mellitus, previously diagnosed.
3. Cardiovascular disease, freshly and previously diagnosed.
4. Regular follow up in diabetic clinic for the last 5 years.

Exclusion criteria
1. Age less than 40 years.
2. Freshly detected patients of Diabetes mellitus.
3. Non Diagnosed patients of cardiovascular diseases.
4. Irregular follow up.
5. Specimen collection
The venous blood was collected for both fasting and post prandial for blood sugar estimation. The fasting blood samples were collected for the estimation of serum Total cholesterol, serum Triglycerides and serum HDL cholesterol estimation. The Random blood samples were collected between 6 to 12 hours in myocardial infarction patients for the estimation of serum CK-MB, serum SGOT and serum Lactate dehydrogenase in the following bulbs,

- Fluoride Bulb – Blood sugar.
- Plain Bulb – Serum Lipid profile, CK-MB, SGOT, and LDH.

All the above mentioned Biochemical investigation were carried out in clinical chemistry laboratory of Biochemistry department of medical college, Baroda. The methods used in the study are in accordance with the facilities available in the clinical Biochemistry Laboratory of Medical college, Baroda. The techniques are recent and used in many Indian laboratories and the results are easy reproducible.

Method used for Estimation of Blood sugar levels
Glucose Oxidase and Peroxidase Method

Principle
The substrate β D-Glucose is oxidized by Glucose oxidase to form gluconic acid and hydrogen peroxide. The hydrogen peroxide, so generated, oxidizes the chromogen system consisting of 4-amino antipyrine and phenolic compounds to a red Quinoneimine dye. The intensity of the colour produced is proportional to the glucose concentration and is measured colorimetrically at 505nm(490-530) or with green filter.

Results

Table 1: Age and Sex Distribution

| Age in Years | No. of Male Patients | No. of Female Patients | Total | Percentage |
|--------------|----------------------|------------------------|-------|------------|
| 40 – 49      | 03                   | -                      | 03    | 10%        |
| 50 – 59      | 09                   | 03                     | 13    | 43.3%      |
| 60 – 69      | 08                   | 08                     | 16    | 40%        |
| 70 – 79      | 02                   | 02                     | 04    | 6.6%       |
| 80 – 89      | 02                   | 08                     | 10    | 30%        |

Table Shows age and sex distribution of all 30 patients. It shows an age range of 40 to 75 years. Mean age of presentation was 60.3 years.

Table 2: Risk factors among 30 patients

| Risk factor     | No. of Patients | Percentage |
|-----------------|-----------------|------------|
| Smoking         | 14              | 46.6%      |
| Hypertension    | 10              | 33.3%      |
| Obesity         | 13              | 43.3%      |
| Family History of Diabetes Mellitus | 9 | 30.0% |
| Alcoholism      | 4               | 13.3%      |
| Tobacco chewing | 5               | 16.6%      |

In the present study among 30 patients, there was either a single or a combination of the above mentioned risk factors were found. The commonest risk factor encountered in this study was smoking. It was encountered in 14 patients (46.6%) of these 14 patients, 8 patients were heavy smokers, smoking more than 20 cigarettes or bides per day. The next most frequent risk factor was hypertension. It was present in 10 patients (33.3%) of these 4 patients were hypertensive for more than 5 years and were on regular treatment. Obesity was present in 13 (43.3%) patients, 10 patients had previous documented evidence of hypercholesteremia. (Blood Cholesterol levels > 250 mg%). Family history of Diabetes Mellitus was present in 9 patients. (30%)
Other risk factors in the form of alcoholism and Tobacco chewing was present in 4 (13.3%) and 5 (16.6%) of patients respectively.
In this study it was found that though the patients were on oral hypoglycaemic drugs and some patients were on Insulin the fasting blood sugar and post prandial blood sugar are significantly high in study groups when compared to control groups ($P < 0.001$).

This suggest that in diabetic subjects at hyperglycemia, there is both a decrease in responsiveness and a decrease in sensitivity to insulin. It is well established that in type 2 diabetes exhibit peripheral insulin resistance in target tissues.

In hyperinsulinemic euglycemic clamp technique, a research method for measuring peripheral insulin resistance, shows that the glucose disposal rate is reduced by at least 50% in subjects with type 2 diabetes $[7]$. 

### Table 3: Comparison between various laboratory parameters in Control [n=30] and Study [n=30] Groups.

| Laboratory parameters | Control Group | Study Group | t   | P value |
|-----------------------|---------------|-------------|-----|---------|
|                       | Mean          | SD          | Mean | SD      |     |
| FBS mg/dl             | 103.0333      | 12.2938     | 164.0667 | 39.4024 | 8.099 | <0.001 |
| PP2BS mg/dl           | 118.0333      | 10.7494     | 212.0000 | 46.2579 | 10.83 | <0.001 |
| TC mg/dl              | 185.1000      | 25.5483     | 230.7333 | 43.1437 | 4.98  | <0.001 |
| TRG mg/dl             | 156.0000      | 31.9633     | 228.3667 | 64.1644 | 5.52  | <0.001 |
| HDL-C mg/dl           | 38.9333       | 5.0646      | 29.4000  | 6.7650  | 6.17  | <0.001 |
| VLDL-C mg/dl          | 31.5333       | 6.4312      | 46.6333  | 12.5931 | 5.84  | <0.001 |
| LDL-C mg/dl           | 114.6333      | 24.4688     | 154.7000 | 46.0163 | 15.04 | <0.001 |
| CK-MB IU/L            | 19.8667       | 6.3449      | 147.5000 | 46.0163 | 15.04 | <0.001 |
| SGOT IU/L             | 27.8000       | 6.0822      | 118.3333 | 70.5341 | 7.004 | <0.001 |
| LDH IU/L              | 360.1667      | 95.5146     | 617.1667 | 135.6845 | 8.48  | <0.001 |

### Discussion

Distribution according to sex showed 73.3% were males and 26.6% were females. There were no female patients below the age of 50 years.

Myocardial infarction can occur at any age and sex, but generally it is a disease of middle age and older individuals: Minitz-Katz \(^8\) reported incidence 66.3% in the age group of 50-59 year. Julien \(et al.\) \(^9\) in their prospective study of
100 unselected patients reported maximum incidence 62.0% in the age group of 50-59 years. In the present study the maximum incidence of acute myocardial infarction was in age range of 52-60 years (53.3). Men are frequently the victims of acute myocardial infarction. This has probably to do with the stressful life and the high incidence of smoking. Probably females are protected in their reproductive period by the sex hormones. In the present study male to female ratio are (2:1). The ratio further decreased with the advancement of age. Men also developed infarction at an earlier age than females. In the present study the average age of presentation was 60.3 years. There were no female patients below the age of 50 years.

The data of the present study regarding age and sex matches with the data published by Mintz-Katz [8] and Julien et al. [9]. This is considered as one of the prime risk factor for CHD. The earlier the age of detection, greater the risk of CHD. Elevated serum cholesterol is associated with risk of CAD. Specifically a 10% increase in serum cholesterol is associated with a 20 – 30% increase in risk of CAD [10]. In men it has been found that 41% variants in CAD mortality was related to variation in serum cholesterol, 32% was related to variation in HDL-C and 55% to variation in ratio of total cholesterol to HDL cholesterol. It is difficult to define a safe basal levels of serum cholesterol. A low risk level, from the point of view of primary prevention should ideally be LDL-C less than 130mg/dl, HDL-C more than 40mg/dl and TRG less than 150mg/dl.

Smoking increases CAD mortality by 50%, it doubles the incidence of CAD, and the risk increases with age and the number of cigarettes smoked. Similar risks have been observed among women. Smoking is a leading preventable cause of death and CAD world wide. Those who quit smoking decrease the risk by 50% in 1-2 years and to normal levels by 5-15 years. Smokers have lower HDL-C levels and high VLDL and triglyceride levels.

Hypertension is a well established risk factor for CAD. Both elevated systolic and diastolic blood pressure are clearly associated with an increased risk of CAD. A 7mm Hg increase in diastolic blood pressure over any base line reading was associated with a 27% increase in CAD risk and 42% increase in stroke risk [11]. Obesity appears to have an independent risk for CAD, even after controlling the other risk factors. A higher BMI is associated with an increase in all the risk factors of CAD. The distribution of body fat may also play a role in the development of CAD, with abdominal adiposity above the umbilicus posing a substantially greater risk in both men and women. A waist circumference of 35 inches in women and 40 inches in men is an easily measured marker of coronary artery disease risk [12].

**Conclusion**

- Serum levels of CK-MB were found significantly elevated in Myocardial Infarction patients with type 2 diabetic individuals when compared to controls. Higher values obtained in patients who suffered cardiovascular complications and mortality.
- SGOT levels were elevated in diabetic study group compared to controls.

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