Original Research Article

Study of association of early-onset coronary artery disease with glucose intolerance and hyperinsulinemia

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Abstract

Background: Indians develop Coronary Artery Disease (CAD) 5 to 10 years earlier than in other populations, and the occurrence of first myocardial infarction before the age of 40 years is 5 to 10 folds higher. Type 2 diabetes and impaired glucose tolerance (IGT) shares several risk factors in common with coronary artery disease (CAD) and an increase in the prevalence of diabetes indirectly implicates an escalating risk of CAD as well. Present study was undertaken to study association of early-onset coronary artery disease with glucose intolerance and hyperinsulinemia in patients attending tertiary care hospital. **Material and Methods:** Present study was a prospective, observational study conducted in subjects, male or female less than 45 years old, coronary artery disease. Glucose intolerance (GI) and serum insulin level were measured. **Results:** In present study, total 42 patients satisfying study criteria were included. Mean age was 42.07 ± 5.78 years. Male (73.81 %) were more than female (26.19 %). Mean body mass index was 23.26 ± 3.66 kg/m^2. In present study, incidence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes mellitus (DM), hyperinsulinemia (>25 µIU/ml) was 9.52 %, 7.14 %, 7.14% and 9.52 % respectively. Total incidence of Glucose intolerance was 14.29 % (6 patients). Hypertension (26.19 %), BMI (> 25 kg/m^2) (26.19 %), Smoking (21.43 %), Dyslipidemia (19.05 %), Family history of CAD (16.67 %) and Family history of diabetes (14.29 %) were major risk factors noted in present study. We noted a statistically significant difference in values of fasting plasma glucose (mg/dl), 2-hour plasma glucose (mg/dl), fasting serum insulin (uIU/ml) and HbA1C between normoglycemic and glucose intolerance patients. **Conclusion:** Glucose intolerance and hyperinsulinemia are associated with early-onset coronary artery disease, early diagnosis by screening of glucose intolerance is strongly recommended in high risk individuals.

Keywords: early-onset coronary artery disease, glucose intolerance, hyperinsulinemia, impaired glucose tolerance

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INTRODUCTION

Cardiovascular disease (CVD) is a global health problem that has reached epidemic proportions in both developed and developing countries.[1] Indians develop Coronary Artery Disease (CAD) 5 to 10 years earlier than in other populations, and the occurrence of first myocardial infarction before the age of 40 years is 5 to 10 folds higher.[2,3] Type 2 diabetes and impaired glucose tolerance (IGT) shares several risk factors in common with coronary artery disease (CAD), such as age, hypertension, dyslipidemia, obesity, physical inactivity, and stress, an increase in the prevalence of diabetes indirectly implicates an escalating risk of CAD as well.[4] While hyperinsulinemia is associated

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with obesity, type 2 diabetes, cardiovascular disease, and subclinical cardiometabolic risk markers, such as dyslipidemia, hypertension, and central adiposity.[5] Plasminogen activator inhibitor (PAI-1) : high levels are reported in Indians in association with hypertriglyceride and hyperinsulinemia. This combination promotes thrombosis by impairing fibrinolysis. Also elevated glucose induces nonenzymatic protein glycosylation, protein kinase C activation, and oxidative stress. Hyperinsulinemia has been associated with collagen deposition and myocardial fibrosis.[6] The potential consequences of early-onset coronary artery disease may have a significant impact on future health and wellbeing due to possible higher psychological and socioeconomic implications. Identifying the major risk factors for early-onset coronary artery disease is of vital significance to develop effective prevention strategies. Present study was undertaken to study association of early-onset coronary artery disease with glucose intolerance and hyperinsulinemia in patients attending tertiary care hospital.

MATERIAL AND METHODS

Present study was a prospective, observational study conducted in patients of early-onset coronary artery disease, admitted in ICCU under Department of Medicine, Bhaarath Medical College and Hospital, Selaiyur. Study duration was 1 year (from October 2019 to September 2020). Institutional ethical committee approval was taken for present study.

Inclusion criteria

The subjects, male or female less than 45 years old, fulfilling any of the following two criteria out of three were included in study.

1. Typical symptoms (Chest discomfort).
2. Typical pattern of ECG (ST segment elevation of ≥ 0.1mv in at least two consecutive leads or fresh left bundle branch block).
3. Elevated enzyme levels (Serum CPKMB two times the upper limit of normal level).

Exclusion criteria

1. History of any oral antidiabetic medications or insulin or known diabetes mellites
2. Associated disorders like primary hyperparathyroidism, chronic kidney disease, liver disease, any chronic illness, malignancy,
3. Subjects of stable and unstable angina
4. Subjects not willing to participate

Study was explained and a written consent was taken for participation. Baseline clinical history, complications, risk factors for coronary artery disease, past illness, clinical examination findings, routine investigations (CBC, RFT's, LFT's, blood sugar profile, lipid profile and Serum CPKMB, chest x-ray) findings were noted. In few cases 2-D echo and Doppler study done were for LVEF and complications of MI. Glucose intolerance (GI) can be defined as dysglycemia that comprises both prediabetes and diabetes. It includes the conditions of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) and diabetes mellitus (DM).[7]All the cases were followed after stabilization (on the 5-7th day of admission) and blood glucose, HbA1c and serum insulin level were measured by commercially available glucose and Insulin IRMA kit (Immune-radiometric assay). Fasting blood sample is taken after an 8 hour overnight fast. FPG levels between 100 and 125 mg/dL (5.6 to 6.9 mmol/L) are diagnostic of IFG. Fasting serum insulin levels were measured and Hyperinsulinemia was (>25 μIU/ml) was noted. In Two-Hour Oral Glucose Tolerance Test (GTT) plasma glucose is measured 2 hours after ingestion of 75 gm of glucose. IGT is diagnosed if plasma glucose (PG) level in the 2-hour sample is between 140 to 199 mg/dL (7.8 to 11.0 mmol/L). DM is diagnosed if the PG is greater than or equal to 200 mg/dl. Data was collected, entered in Microsoft excel sheet. Statistical analysis was done using SPSS 21. Data was presented in percentage and mean ± SD. Continuous clinical characteristics in both group were compared by unpaired t-test and categorical variables in both groups were compared by using Chi square statistics, statistical significance was considered when $p<0.05$.

RESULTS

In present study, total 42 patients satisfying study criteria were included. Mean age was 42.07 ± 5.78 years. Male (73.81 %) were more than female (26.19 %). Mean body mass index was 23.26 ± 3.66 kg/m^2. In present study, incidence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes mellitus (DM), hyperinsulinemia (>25 μIU/ml) was 9.52 %, 7.14 %, 7.14% and 9.52 % respectively. Total incidence of Glucose intolerance was 14.29 % (6 patients). Hypertension (26.19 %), BMI (> 25 kg/m^2) (26.19 %), Smoking (21.43 %), Dyslipidemia (19.05 %), Family history of CAD (16.67 %) and Family history of diabetes (14.29 %) were major risk factors noted in present study

Table 1: General characteristics

Variables	No. of patients / Mean ± SD (N = 42)	Percentage (%)
Age (years)	42.07 ± 5.78	
Gender		
MALE	31	73.81
FEMALE	11	26.19
Body mass index (kg/m2)	23.26 ± 3.66	
Waist circumference (cm)	83.78 ± 4.98	
Impaired fasting glucose (IFG)	4	9.52
Impaired glucose tolerance (IGT)	3	7.14
Diabetes mellitus (DM)	3	7.14
Hyperinsulinemia (>25 µIU/ml)	4	9.52
Risk factors		
Hypertension	11	26.19
BMI (> 25 kg/m^2)	11	26.19
Smoking	9	21.43
Dyslipidemia	8	19.05
Family history of CAD	7	16.67
Family history of diabetes	6	14.29

We noted a statistically significant difference in values of fasting plasma glucose (mg/dl), 2-hour plasma glucose (mg/dl), fasting serum insulin (uIU/ml) and HbA1C between normoglycemic and glucose intolerance patients.

Table 2: Comparison of Glycaemic parameters

Variable	Glucose intolerance (n = 6)	Normoglycemic (n = 36)	p-value	Significance
Fasting Plasma Glucose (mg/dl)	100.24 ± 9.18	84.27 ± 7.44	<0.001	Significant
2-hour Plasma Glucose (mg/dl)	153.87 ± 13.56	124.38 ± 11.46	<0.001	Significant
Fasting serum Insulin (uIU/ml)	18.26 ± 12.14	10.81 ± 8.29	<0.001	Significant
HbA1C	8.66 ± 2.43	5.79 ± 0.79	<0.001	Significant

DISCUSSION

Prediabetes is an intermediate stage between normal glucose levels and the clinical entity of type 2 diabetes (T2D), defined as Impaired Fasting Glucose (IFG) (Fasting plasma glucose 100 - 125 mg/dl) and Impaired Glucose Tolerance (IGT) [2 hr plasma glucose ≥140 and ≤199 mg/dl] after ingesting 75 g of glucose (OGTT); or a combination of both.[8] Asymptomatic hyperglycaemia is a risk factor for cardiovascular disease (CVD) and hyperglycaemia can develop during an acute MI, even in patients without diabetes, which may be caused by an increase in catecholamines, a reduction in the release of insulin, development of insulin resistance and increases in cortisol and growth hormone.[9] Adverse consequences from hyperglycemia may reflect effects of glucose as well as hyperinsulinemia. Glycemic effects include elevations in reactive oxygen species and formation of advanced glycation products. Hyperinsulinemia has been associated with mitogenic effects on vascular smooth muscle cells.[10,11] With India undergoing rapid industrialization and urbanization, the consequent changes in the form of sedentary lifestyle are rampant. The India State-Level Disease Burden Initiative has reported that, although the prevalence of cardiovascular disease risk factors varied considerably across the states of India, the prevalence of high systolic blood pressure, high total cholesterol, and high fasting plasma glucose increased across all state groups since 1990.[12] In India, most common risk factor associated with young CAD seems to be smoking. [13] Smoking in presence of additional risk factors like diabetes, hypertension and obesity predispose a young individual to increased risk of future acute coronary events.[13] Similar findings were noted in present study. In a prospective study, fasting immune reactive insulin levels beyond 20 µIU/ml was independently associated with an incidence of CAD, subjects with high insulin levels were at five to sixfold risk for developing CAD.[14] In another cross-sectional study, they observed that an elevated insulin level was independently associated with angiographically determined CAD.[15] Srinivasan M studied subjects who underwent coronary angiogram for an evaluation of CAD, relation between the cardiovascular risk factors and major adverse cardiac events (MACE). After adjustment for potential confounders hyperinsulinemia (>20 µIU/ml) was significantly associated with MACE. Basal hyperinsulinemia beyond >20 µIU/ml, strongly predicts adverse cardiac events at 1 year in type 2 diabetes mellitus.[16] Hyperinsulinemia, insulin resistance, and the higher rate of prevalence of metabolic syndrome in people with type 2 diabetes were attributed to high coronary risk in south Asians.[17] Several longitudinal studies have shown that, hyperinsulinemia is

associated with new cardiac events in general population and high fasting insulin levels are directly associated with carotid intima thickness and arterial wall stiffness even after adjusting for hypertension, dyslipidemia and obesity..[18,19] Hyperinsulinemia, impaired glucose intolerance are common condition often associated with T2DM in which insulin levels exceed the normal range. However, until the insulin levels reach peak values, there does not appear to be a risk of developing severe vascular complications.[20] Apart from disturbance in glucose metabolism, there are several behavioural risk factors such as tobacco use, unhealthy diet, obesity, physical inactivity and harmful use of alcohol and incidence of CVD can be controlled by addressing these factors.

CONCLUSION

Glucose intolerance and hyperinsulinemia are associated with early-onset coronary artery disease, early diagnosis by screening of glucose intolerance is strongly recommended in high risk individuals.

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