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STUDY OF RISK FACTORS OF CORONARY ARTERY DISEASE IN TYPE 2 DIABETIC PATIENTS

Medicine

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ABSTRACT

Aim- To study risk factors of coronary artery disease in type 2 diabetic patients

Materials and Methods- Two groups of diabetic patients ,total 88 patients were studied for common risk factors for diabetes and coronary artery disease, Group A (Patients with coronary artery disease-52) and Group B (Patients without coronary artery disease-36)

Results and discussion: The present study shows that various risk factors like hyperglycemia, dyslipidemia, hypertension, obesity shows positive association with development of CAD in patients with type 2 diabetes, with elevated LDL and low HDL levels having the highest odd's ratio. The findings of this study can aid in the early and regular screening as well as aggressive management of these conventional risk factors in diabetic patients.

KEYWORDS

INTRODUCTION

Atherosclerosis is major contributor to the morbidity and mortality observed in Diabetes Mellitus. The development of diabetes related atherosclerosis follows the same histologic course as atherosclerosis in non-diabetic patients.

Atherosclerotic plaques in the presence of diabetes generally have increased calcification, necrotic cores, receptors for advanced glycosylation end products (RAGE) as well as macrophage and T-cell infiltration.

There is also a higher incidence of healed plaque rupture and vascular remodelling. These features can potentially contribute to the more severe atherosclerosis and a higher incidence of acute coronary events. The development of atherosclerosis is a result of:

- Chronic Hyperglycaemia
- Secondary insulin resistance
- Dyslipidemia
- Hypercoagulability
- Endothelin-1
- Impaired response to injury.

Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications. Significant evidence exists that supports a range of interventions to improve diabetes outcomes. According to World health statistics 2012 report 1 in 6 adults is obese, 1 in 10 adults is diabetic and 1 in 3 is hypertensive[1]. Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035. The prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population[2]. The WHO estimated that there were 19.4 million persons with diabetes in India in 1995 and that this number is likely to be 69.9 million in 2025. Type 2 diabetes amongst Indians occurs at a younger age, the age at diagnosis being a decade earlier than in the West. Body mass index is lower by 4 kg/m2 for males and 6 kg/m2 for females. However abdominal obesity with increased waist to hip ratio is more common. It is projected that equal number of diabetics are undetected for a long time and hence may present with micro-vascular and macro-vascular complications at the time of diagnosis.[3]

Coronary artery disease is the leading cause of death in both men and women among diabetics. It may be asymptomatic in many of diabetic individuals. The risk for CHD can be predicted based on the traditional risk factors included in the Framingham risk score (age, sex, blood pressure, serum total cholesterol, low density lipoprotein [LDL] or high density lipoprotein [HDL] level, cigarette smoking and diabetes)[4].

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

RISK FACTORS FOR CORONARY ARTERY DISEASE[5,6]

Risk factors multiply, with two factors increasing the risk of atherosclerosis 4 times. Hyperlipidaemia, hypertension, uncontrolled diabetes and cigarette smoking together increases the risk 7 times.

Modifiable Risk Factors:

- Diabetes or Impaired glucose tolerance
- Dyslipoproteinemia 1. High LDL and VLDL. 2. Low HDL-C 3. An LDL: HDL ratio greater than 3:1
- Tobacco smoking, increases risk by 200% after several pack years.
- Hypertension
- Elevated serum C-reactive protein
- Vitamin B_{12} deficiency
- Obesity (in particular central obesity, also referred to as abdominal or male type obesity)
- Postmenopausal Oestrogen deficiency
- High intake of saturated fat (may raise total and LDL cholesterol) Intake of trans fat (may raise total and LDL cholesterol while lowering HDL cholesterol)
- Elevated serum levels of triglycerides
- Elevated serum levels of homocysteine and uric acid
- Elevated serum fibrinogen concentrations
- Chronic systemic inflammation as reflected by upper normal WBC concentrations, elevated hs-CRP and many other blood chemistry markers, most only research level at present, not clinically done.
- Hyperthyroidism (an over-active thyroid)

Infections

1. Chlamydia pneumoniae infection.

2. Herpes virus infection of arterial smooth muscle cells (cholesteryl ester accumulation).
3. Cytomegalovirus (CMV) infection.

Non-modifiable Risk Factors:

- Advanced age
- Male sex
- Having close relatives who have had some complication (e.g. CAD or stroke)
- Gene abnormalities, e.g. familial hypercholesterolemia
- Elevated serum lipoprotein (a) concentrations

AIM OF THE STUDY

To study risk factors of Coronary Artery Disease in type 2 diabetic patients.

MATERIAL AND METHODS

The present study was carried out in the Department of Medicine in a tertiary care hospital in Ahmedabad.

Study design – Prospective clinical study *Study duration* – JANUARY 2017 to NOVEMBER 2017

Total number of Patients - 88

***Inclusion Criteria*:**

- Age: 35-75 years
- Diabetes Mellitus Type 2 diagnosed as per WHO criteria.

***Exclusion criteria*:**

- Age < 35 or >75 years.
- Past history of Ischemic heart disease
- Patients on lipid lowering agents or Aspirin

***Methods*:**

Total 88 diabetic patients, coming at Diabetes OPD, Civil Hospital Ahmedabad were selected and underwent electrocardiography (ECG). Patients who had ST-T abnormalities or Q waves or rhythm abnormalities were selected and underwent Two dimensional Echocardiography (2D-ECHO) by experienced cardiologists using high resolution M-mode ECHO machine. Both global and regional wall motion abnormalities of the left ventricle or evidence of left ventricular dysfunction were considered as positive result.

Those who had negative results in ECGs and 2D- ECHO underwent treadmill testing. Results were interpreted by experienced cardiologists. Flat or down-sloping depression of the ST segment >0.1 mV below baseline (i.e., the PR segment) and lasting longer than 0.08 second were considered diagnostic and those who had negative TMT (n=42) were requested for coronary angiography performed by cardiologists at U.N. Mehta cardiology institute. Only 8 patients were willing for angiography out of them 6 were found >50% stenosis in epicardial coronary arteries.

All the others were considered (n=36) as they did not have IHD and they were taken as controls. The study group was divided into 2 subgroups:

- Group A: Patients with evidence of CAD
- Group B: Patients without any evidence of CAD

OBSERVATION AND RESULTS

In present study a total of 88 patients were taken out of which 52 were Type-2 Diabetic patients with evidence of CAD and 36 were controls. The patients were followed up from January 2017 to November 2017. The observations made in the present study are summarized as follows:

Table:1-Age and sex wise distribution of Diabetic Cases with evidence of CAD

Age	MALE	FEMALE	TOTAL
<40	1	1	2
41-50	2	5	7
51-60	10	8	18
61-70	14	7	21
>70	2	2	4
TOTAL	29	23	52

Table:2-Age and sex wise distribution of Diabetic Cases without evidence of CAD.

Age	MALE	FEMALE	TOTAL
<40	4	2	6
41-50	9	6	15
51-60	4	4	8
61-70	2	3	5
>70	1	1	2
TOTAL	20	16	36

Out of these 52 diabetic patients with CAD, 29 were males and 23 patients were females. Majority of the patients (21) were within the age group of 61 to 70 years of age. 18 patients were within the age group of 51 to 60.

The total mean age in present study was 56.82 years. Mean age for male is 58.2 years and for female is 55.08 years.

The number of patients in the age group of >70 were 4. This can be explained due to the fact that as the long duration of diabetes is associated with higher number of both Micro-vascular and Macro-vascular complications and this results in increased mortality with age.

Out of these 36 diabetic patients without ischemic heart disease 20 were males and 16 patients were females. Majority of the patients 15 were within the age group of 41 to 50 years of age. 13 patients were within the age group of 51 to 70.

The total mean age of diabetes patients without ischemic heart disease in present study was 50.06 years. Mean age for male is 48.45 years and for female is 52.06 years.

This would explain that ischemic heart disease risk increase with increasing age (Mean age of CAD population> Mean age of population without CAD) [p<0.05]

Table-3: HbA1c as a risk factor

HbA1c %	No of diabetic patients with evidence of CAD(Group A)	No of diabetic patients without evidence of CAD(Group B)
6-6.9	6	19
7-8.9	13	12
>9	16	5
Total	52	36

The mean HbA1c of our study group A is 8.18, and of control group was 6.84

The patients with well controlled diabetes (HbA1c<7) had low risk of coronary artery disease. Those with poor control of diabetes with HbA1c >7 have higher risk of coronary atherosclerosis with asymptomatic CAD due to diabetic autonomic neuropathy (p<0.005).

This shows that poorly controlled diabetes increases the risk more severe atherosclerosis and a higher incidence of acute adverse events as a result of chronic hyperglycaemia, secondary insulin resistance, dyslipidaemia and hypercoagulability.

This positive co relation between HbA1c and CAD is supported with a significant p-value of 0.01.

Table 4 :BMI as a risk factor

BMI		No. of diabetic patients with evidence of CAD (Group A)	No. of diabetic patients without evidence of CAD(Group B)
15-19.99	Underweight	0	2
20-24.99	Normal	11	18
25-29.99	Overweight	29	12
30-34.99	Obesity	10	4
>35	Morbid obesity	2	0
Total		52	36

11 patients out of 52 diabetics had BODY MASS INDEX less than 25, the rest 41 had BMI more than or equal to 25, and out of which 29

patients were overweight, 10 patients were obese and 2 were morbidly obese.

In control group, 20 patients out of 36 are within normal BMI range, only 16 are in the overweight or obese group.

As defined by the World Health Organization and the National Cholesterol Education Programme (NCEP), on the basis of blood glucose, hypertension, dyslipidaemia, body mass index, waist / hip ratio, and urinary albumin excretion, The Metabolic Syndrome is associated with coronary atherosclerosis after adjustment for other risk factors and in my study majority of patients were above the normal range of BMI, thus significantly increasing the risk for the same.

Mean BMI is 27.72 $Kg/^{m2}$ in patients with asymptomatic IHD (Group A) and 23.87 Kg/m2 in control (Group B).

Odds ratio is 4.66 suggestive of patients having BMI ≥ 25 have 4.66 times more risk of developing CAD than patients having low BMI with same risk factors.

The Mean BMI of the study group was 27.72 Kg/m2 with S.D. of 3.57 as compared to Mean BMI of the control group which is 23.87 with S.D of 2.69. The mean BMI of the study group is statistically significant with "p value" of 0.05.

This significant difference points to the fact that diabetic patients tend to have other components of metabolic syndrome too, thus increasing their morbidity.

Table 5: Hypertension as a risk factor

Hypertension	No. of diabetic patients with evidence of CAD (Group A)	No. of diabetic patients without evidence of CAD (Group B)
Hypertensives (BP>=140/90)	23(44.23%)	4(11.11%)
Normotensives(BP < 140/90)	29(55.77%)	32(88.89%)
Total	52	36

The odds ratio is 6.35, which suggests that hypertension is an independent risk factor for CAD in diabetics.

Thus CAD has direct correlation with elevated blood pressures in patients with diabetes mellitus.

Table 6(A-D) : Lipid profile as a risk factor
6A = Cholesterol

Cholesterol (mg/dl)	No. of diabetic patients with evidence of CAD (Group A)			No. of diabetic patients without evidence of CAD (Group B)		
	Male	Female	Total	Male	Female	Total
<200	5	3	8	12	7	19
200-240	20	14	34	5	6	11
>240	4	6	10	3	3	6
Total	29	23	52	20	16	36

Mean cholesterol for study population is 213.84 mg/dl and the SD is 25.02. The population mean is 192.56mg/dl.

The odds ratio is 6.15. Thus hypercholesterolemia is an independent risk factor for CAD in diabetics.

6B = Triglyceride

Triglyceride (mg/dl)	No. of diabetic patients with evidence of CAD (Group A)			No. of diabetic patients without evidence of CAD (Group B)		
	Male	Female	Total	Male	Female	Total
<150	3	5	8	10	6	16
151-199	10	6	16	7	5	12
>200	16	12	28	3	5	8
Total	29	23	52	20	16	36

Mean cholesterol for study population is 208.59mg/dl with SD of 50.01. The population mean is 152.69 mg/dl.

The odds ratio is 4.08. Thus hypertriglyceridemia is an independent risk factor for CAD in diabetics.

6C = LDL

LDL (mg/dl)	No. of diabetic patients with evidence of CAD (Group A)			No. of diabetic patients without evidence of CAD (Group B)		
	Male	Female	Total	Male	Female	Total
<100	0	2	2	12	6	18
100-129	6	6	12	7	7	14
>130	23	15	38	1	3	4
Total	29	23	52	20	16	36

Mean cholesterol for study population is 154.29 mg/dl. The SD is 27.14. The population mean is 102.65 mg/dl.

The odds ratio is 21.7. Thus raised LDL has a direct correlation for CAD in diabetics.

6D = HDL

HDL (mg/dl)	No. of diabetic patients with evidence of CAD (Group A)			No. of diabetic patients without evidence of CAD (Group B)		
	Male	Female	Total	Male	Female	Total
<40	24	20	44	4	2	6
≥40	5	3	8	16	14	30
Total	29	23	52	20	16	36

Mean cholesterol for study population is 38.46 mg/dl. The SD is 1.53. The population mean is 43.56 mg/dl.

The odds ratio is 33. Thus low HDL has a direct correlation for CAD in diabetics.

SUMMARY:

In present study a total of 88 patients were taken out of which 52 were Type−2 diabetic patients with evidence of Coronary Artery Disease and 36 were controls, i.e., without any evidence of CAD. The patients were followed up from January 2017 to November 2017.

The total mean age in present study was 56.82 years. Mean age for male is 58.2 years and for female is 55.08 years.

The commonest age group is 61 to 70 years making 40.38% of total CAD cases.

Out of these 52 diabetic patients with coronary artery disease 29 were males and 23 patients were females, so sex ratio in present study is 1.26:1.

The mean HbA1c of our study group A is 8.18 while control group is 6.84. This shows that poorly controlled diabetes increases the risk of more severe atherosclerosis and a higher incidence of acute coronary events as a result of Chronic Hyperglycemia, Secondary insulin resistance, Dyslipidemia and Hypercoagulability. This positive co relation between HbA1c and CAD is supported with a significant p-value of <0.05.

11 patients out of 52 diabetics had BODY MASS INDEX less than 25, the rest 41 had BMI more than or equal to 25, and out of which 29 patients were overweight, 10 patients were obese and 2 were morbidly obese. Majority of patients in the study were above the normal range of BMI, thereby establishing a positive association with coronary artery disease.

The Mean BMI of the study group was 27.72 Kg/m2 with S.D. of 3.57, as compared to Mean BMI of the control group which is 23.87 with S.D of 2.69. Odds ratio is 4.66 suggestive of patients having BMI ≥ 25 have 4.66 times more risk of developing CAD than patients having low BMI with same risk factors.

In our study 23 patients were hypertensive. Odds ratio for hypertension is 6.35 suggesting that hypertension is an independent risk factor for coronary atherosclerosis. (p- Value< 0.05)

Mean total cholesterol level for the study population is 213.84 mg/dL

and standard deviation (SD) is 25.02 .Range is 213.84 ± 12.51 mg/dL. Odds ratio is 6.15. It suggests that hypercholesterolemia (S. Cholesterol ≥ 200 mg/dL) is an independent risk factor for coronary artery disease.

Mean Triglyceride for study population is 208.59 mg/dL and standard deviation (SD) is 50.01 .Range is 208.59 ± 25.01 mg/dL. Odds ratio is 4.08. It suggests that hypertriglyceridemia (S. TG ≥ 200 mg/dL) have direct co−relation with coronary artery disease.

Mean LDL for study population is 154.23 mg/dL and standard deviation (SD) is 27.14 .Range is 154.23 ± 13.57 mg/dL. Odds ratio is 21.7. It suggests that raised LDL (S. LDL ≥ 130 mg/dL) have direct co−relation with coronary artery disease.

Mean HDL for study population is 38.46 mg/dL and standard deviation (SD) is 1.53 .Range is 38.46 ± 0.76 mg/dL. Odds ratio is 33. It suggests that low HDL (S. HDL ≤ 40 mg/dL) have direct co−relation with CAD.

Table 7: Odds Ratio of Various Risk Factors:

RISK FACTOR	ODDS RATIO
Uncontrolled HbA1C	1.87
Hypertension	6.35
Overweight/ Obesity	4.6
Hypercholesterolemia	6.15
Hypertriglyceridemia	4.0
Elevated LDL-C levels	21.7
Low HDL-C levels	33

CONCLUSION:

This study aims to establish a positive relationship between the various metabolic abnormalities seen in diabetic patients and the high incidence of coronary artery disease in these patients. There is a particularly high prevalence of the metabolic syndrome in patients with Diabetes Mellitus, with insulin resistance playing a predominant role in the pathophysiology. The metabolic syndrome is a conglomerate of several risk-factors often existing together, that culminate into increased vulnerability of patients to developing coronary artery disease.

The study confirms the association of uncontrolled diabetes, Hypertension, Obesity and Dyslipidaemia in diabetic patients to coronary artery disease. Among these risk factors, the Odds ratio was highest with elevated LDL-C and decreased LDL-C levels.

Thus, patients with type 2 diabetes mellitus should be regularly screened for hypertension, obesity and dyslipidaemia- which contribute to the development of the metabolic syndrome and then should be aggressively managed for the same.

Also, a high level of suspicion should be maintained for presence of ischemic heart disease in type 2 diabetics because of both, the high incidence of co-existing conditions that are individual risk factors for CAD as well as the fact that diabetics are particularly vulnerable to developing asymptomatic coronary artery disease.

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