ORIGINAL ARTICLE

Co-relation Between Total Cholesterol, High Density Lipoprotein, Low Density Lipoprotein and Glycosylated Haemoglobin (HbA1c) in Diabetic Patients with Acute Coronary Syndrome (ACS)

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Abstract

Background: Patients with diabetes & dyslipidaemia are at increased risk of developing coronary artery disease that many time manifests as life threatening ACS.

Aim: To study co-relation between HbA1c &total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) in diabetic patients with acute coronary syndrome and also their co-relationship with severity of ACS independently.

Materials & method: Blood samples of 51 known diabetic patients presented to emergency with ACS were sent for HbA1c & lipid profile estimation. All patients underwent coronary angiography. Obtained results were statistically analysed & co-related.

Results: Patients were divided as having: 1. HDL <40, >40; 2. LDL <100, >100; 3. Total cholesterol <200, >200; 4. HbA1c 6.5-8.4, >8.4; 5. Single vessel disease (SVD) / multi vessel disease (MVD). Statistically significant direct co-relationship was found between HbA1c, LDL, Total cholesterol, ACS severity (SVD/MVD) & inverse co-relationship with HDL.

Conclusion: Severity & incidence of ACS in diabetic patients can be minimised by maintaining adequate glycaemic control & also by keeping circulating lipids under control.

Introduction

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with myocardial ischemia and covers the spectrum of clinical conditions ranging from unstable angina, non ST segment elevated myocardial infarction (NSTEMI) and ST segment elevated MI (STEMI).[1]

Potentially modifiable risk factors for ACS - smoking, diabetes, hypertension, dyslipidaemia, obesity, psychosocial factors, lack of exercise, and a diet low in fruit and vegetables along with little or no alcohol consumption.[2]

HbA1c is a biomarker reflecting both fasting and PP plasma glucose concentration over preceding 3 months and also it has been regarded as an important tool in management of diabetes.[3] HbA1c can be used to diagnose diabetes and the diagnosis can be made if HbA1c level is >6.5%.[4] Diagnosis should be confirmed with a repeat HbA1c test, unless clinical symptoms and plasma glucose levels >200 mg/dl are present in which case further testing is not required. HbA1c just below 6.5% may indicate the presence of intermediate hyperglycemia. ADA has suggested HbA1c between 5.7-6.4% as the high risk range.[5]

Dyslipidemia is a well established risk factor for the development of coronary artery disease, and this has been demonstrated in several clinical and epidemiological studies.[6-8] High plasma low-density lipoprotein cholesterol concentrations are directly correlated with the development of coronary artery disease[9] and low high density lipoprotein cholesterol concentration have been pointed out as one of the strongest independent risk factor for CAD.[10]

Levels of LDL, Total and HDL cholesterol:

LDL CHOLESTEROL <100 - Optimal, 100-129 - Near or above optimal, 130-159 -Borderline high, 160-189 - High, >190 - Very high. Total cholesterol <200 - Desirable, 200-239 - Borderline high, >240 - High. HDL cholesterol <40 - Low >60 - High[11]. Three categories of risk that modify LDL cholesterol goals:

Risk categories	LDL goal (mg/dl)
- CHD and Risk equivalents*	<100
- Multiple(2+) risk factors**	<130
0-1 risk factor	<160

*Diabetes is regarded as a coronary heart disease risk equivalent. **Risk factors-cigarette smoking, hypertension, low HDL, family history of premature CHD (in male first-degree relative <55 years of age, in female first-degree relative <65 years), age (men >45 years; women >55 years) .[11]

Significantly increased levels of cholesterol and lipids are also seen in type 2 diabetic patients with CAD as compared to diabetic patients without CAD. It has been observed that there is a direct correlation between HbA1c and the severity of CAD in diabetic patients.[12]

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Table 1: Glycosylated haemoglobin (HbA1c) and coronary vessels involved

		Coronary vessels involved				Total	
		Single vessel		Multi-vessel			
		N	%	n	%	n	%
HbA_{1c}	6.5 - 8.4	31	79.5	0	0.0	31	60.8
	8.5+	8	20.5	12	100.0	20	39.2
Total		39	100.0	12	100.0	51	100.0
Mean		7.67		10.78		8.40	
Std. deviation		0.71		1.44		1.62	
Independent samples mann-whitney U-test p-value						<0.001	

Table 2: High density lipoprotein (in mg/dl) and coronary vessels involved

		Coronary vessels involved				Total	
		Single vessel		Multi-vessel			
		n	%	n	%	N	%
HDL	< 40	19	48.7	11	91.7	30	58.8
	40+	20	51.3	1	8.3	21	41.2
Total		39	100.0	12	100.0	51	100.0
Mean		41.62		25.92		37.92	
Std. deviation		11.12		8.67		12.48	
Independent samples mann-whitney U-test p-value						<0.001	

Table 3: Low density lipoprotein (in mg/dl) and coronary vessels involved

		Coronary vessels involved				Total	
		Single vessel		Multi-vessel			
		n	%	n	%	n	%
LDL	< 100	24	61.5	0	0	24	47.1
	100+	15	38.5	12	100.0	27	52.9
Total		39	100.0	12	100.0	51	100.0
Mean		96.15		162.83		111.84	
Std. deviation		31.79		36.74		43.37	
Independent samples mann-whitney U-test p-value						<0.001	

Table 4: Total cholesterol (in mg/dl) and coronary vessel involved

		Coronary vessels involved				Total	
		Single vessel		Multi-vessel			
		n	%	n	%	n	%
Cholesterol	< 200	34	87.2	4	33.3	38	74.5
	200 - 239	3	7.7	6	50.0	9	17.6
	240+	2	5.1	2	16.7	4	7.8
Total		39	100.0	12	100.0	51	100.0
Mean		164.13		216.33		176.41	
Std. Deviation		33.44		41.22		41.52	
Independent samples mann-whitney U-test p-value						<0.001	

Materials and Methods

The study was cross-sectional study done from 1/1/2015 to 31/5/2016.Diabetic patients presented in cardiology unit of medicine at SRMSIMS, Bareilly and were diagnosed to have acute coronary syndrome were taken in study.

Inclusion criteria: Known patients of diabetes mellitus on treatment with either insulin or oral drugs or both, presenting with acute coronary syndrome, in emergency.

Exclusion criteria: Patient already on hypolipidemic drugs, Old case of coronary artery disease, newly diagnosed cases of diabetes mellitus, Patients with conditions confounding lipid profile measurement[13] such as known case of hypothyroidism, obstructive liver disease, chronic renal disease, nephrotic syndrome, Patient on medication such as estrogen, progestin, anabolic steroids, corticosteroids, retinoid, cyclosporine& anti- retroviral medication.

Sample size: 51 diabetic patients with acute coronary syndrome.

Methodology of data collection: Diabetic patients presented in cardiology unit of medicine at SRMSIMS, Bareilly with symptoms of myocardial ischemia or atypical symptoms of ACS were taken for study. Detailed history of present illness with past history, personal history, family history was taken. General and systemic examination was done. Following which written consent was taken and patient was investigated with ECG, Cardiac troponins, Glycosylated haemoglobin, Fasting lipid profile, Liver function tests, Kidney function tests, Complete blood count, TSH estimation.

Diagnosis of ACS was made on the basis of ECG, cardiac troponins and clinical features.

All these patients undergone coronary angiography to find presence of whether single-vessel or multi-vessel disease on ARTIS-ZEE FLOOR CATH LAB OF SIEMENS.

HbA1c estimation was done by enzymatic assay method on automated analyser.

Total cholesterol was measured using liquid cholesterol reagent set for determination of total cholesterol based on enzymatic method using cholesterol esterase, cholesterol oxidase and peroxidase on automated analyser, Triglycerides were measured by glycerokinase peroxidase- peroxidase method on automated analyser, HDL cholesterol was measured by phosphotungstic acid method on automated analyser, LDL was calculated using formula total cholesterol – (VLDL + HDL), VLDL was calculated as triglyceride/5.Automated analyser used was of Shenzhen Mindray Bio-Medical Electronics.

Statistical Analysis: Data was entered in Microsoft Excel 2010 and statistical analysis was done using IBM SPSS V 20.00. Categorical variables were analysed using proportion and percentages. Continuous variables were summarised by mean and standard deviation and association test was done by parametric tests.

Results

Significant co-relation between HbA1c and ACS severity depicted in form of single/multi-vessel disease. Mean HbA1c of patients with single-vessel disease was 7.67±0.71 and of patients with multi-vessel disease was 10.78±1.44 (Table 1).

Significant inverse co-relation was also found between HDL and ACS severity with mean HDL in SVD patients 41.62±11.12 and in patients with MVD it was 25.92±8.67 (Table 2).

Significant co-relation was also found between LDL and ACS severity with mean LDL in SVD patients 96.15±31.79 and in patients with MVD it was 162.83±36.74 (Table 3).

Significant co-relation was also found between total cholesterol and ACS severity. With mean total cholesterol 164.13±33.44 in patients with SVD and mean 216.33±41.22 in patients with MVD (Table 4).

Significant direct co-relation was also found between HbA1c and total cholesterol, LDL and inverse significant co-relation with HDL (Table 5).

Discussion

Our study showed direct co-relation

of HbA1c with ACS severity in the study patients. Similar type of relation was also observed in study "HbA1c level correlation as a predictor of coronary artery disease and its severity in patients undergoing coronary angiography" conducted by Baligar BD et al[14] in 2016 on 100 patients presented with ACS. Coronary angiography was performed on all patients. Relationship between HbA1c and no of vessels involved was evaluated and it was found that most of the patients with single vessel disease had their HbA1c between 6.5%-8.5% and most patients with multi-vessel disease had their HbA1c level above 8.5%. In the end of study it was concluded that HbA1c may be a useful indicator for CAD risk evaluation.

In our study significant inverse relationship was found between HDL-cholesterol and ACS. In the study "Prevalence of conventional risk factors and lipid profiles in with ACS and significant coronary disease" by Gonzalez-Pacheco H et al[15] in 2014 on 3,447 patients with a diagnosis of ACS and significant CAD with stenosis > or =50%, as shown in CAG. Lipid profile was sent in first 24 hours of admission and evaluated along with conventional risk factors such as smoking, dyslipidemia, diabetes and smoking. The lipid profile analysis revealed that 85.1% of patients had some type of dyslipidemia, and most frequent was low level of HDL-cholesterol.

Our study also showed significant co-relationship between LDL-cholesterol level and ACS. In a study conducted by "The lipid research clinics coronary primary prevention trial results"[16] in 1984 showed that reducing total cholesterol by lowering LDL-C levels can diminish the incidence of CHD mortality and morbidity in men at high risk of CHD because of raised LDL-C. The trial provides strong evidence for a causal role for LDL-C in pathogenesis of CHD.

Our study also found significant relationship between total cholesterol and ACS, probably attributable to high LDL-C and low HDL-C. Results of our study showed mean cholesterol of >200 mg/dl in patients with multi-vessel disease which was considered high and risk factor for CAD as per adult treatment panel III(ATP III) guidelines.

Our study showed significant co-relationship between HbA1c levels and LDL, total cholesterol and also significant inverse relationship with HDL. Similar type of co-relation has also been found in study conducted by Cho SW et al[17] in 2016 on 708 patients who visited OPD and followed for a mean period of 28.5 months. Patients were divided in two groups, patients without major adverse cardiovascular event and patients with major adverse cardiovascular event, which included cardiac death, acute MI and newly diagnosed coronary heart disease. HbA1c and lipid profiles between the groups were compared. It was found that patients with major adverse cardiovascular events had significantly higher HbA1c, lower HDL when compared with patients with no adverse events. Significant inverse co-relationship was found between HbA1c and HDL-C on statistical analysis. It was concluded that poor glycemic control and low HDL-C co-relate with each other and HbA1c could serve as simple and useful marker and predictor for lipid profile and major adverse cardiovascular events.

Conclusion

From this study we conclude that severity of ACS, as depicted in form of single or multi-vessel disease in coronary angiography, directly co-relates with poor glycaemic control depicted in form of raised HbA1c.

Severity of ACS also co-relates directly with deranged lipid profile like raised LDL, triglyceride/HDL ratio, total cholesterol and decreased HDL.

There is also significant co-relationship between poor glycaemic control and deranged lipid profile. Patients with raised HbA1c were also found to have deranged lipid profile and in result more severe ACS.

Thus we conclude that early therapeutic interventions, aiming to stabilize blood glucose levels along with reduction HbA1c and LDL, total cholesterol and to increase HDL, significantly reduce cardiovascular events and mortality in patients with diabetes.

Limitations of study

The sample size of patients in our study was less, further study regarding our topic is needed with more study subjects. We also did not studied other well known risk factors for ACS like smoking, lifestyle (sedentary/heavy working), dietary habits etc.

Table 5: Correlation between Glycosylated haemoglobin and Lipid profile

Total Cholesterol	Pearson Correlation	0.476
	P-value	<0.001
HDL	Pearson Correlation	-0.65
	P-value	<0.001
LDL	Pearson Correlation	0.627
	P-value	<0.001

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