

High Density Lipoprotein Cholesterol as a Risk Factor of Coronary Artery Diseases in Young Western Indians: A Comparison with Other Lipid Markers

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ABSTRACT

Introduction: Dyslipidemia – a modifiable risk factor of Coronary Artery Diseases (CAD) is often subjected to ethnic variations. Different communities are known to possess different pattern of lipid abnormalities and study of it is highly required in order to form various preventive strategies.

Aim: To compare the prevalence of dyslipidemias in healthy control versus young CAD patients from Western India. We also seek to assess the strength of each associated dyslipidemia and propose a most suited risk factor for this community.

Materials and Methods: In this single centric, prospective and case control study 200 subjects (100 patients with CAD & 100 healthy volunteer) were enrolled. Fasting blood sample were collected from the antecubital vein of the subjects under sterile conditions. Lipid profile parameters such as Total Cholesterol (TC), Triglyceride (TG), Total Lipid (TL), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), and Very Low Density Lipoprotein Cholesterol (VLDL), Lipoprotein (a) were measured.

Statistical Analysis: Comparison between normally distributed data was performed using student's t-test,

whereas, normally not distributed data was assessed using Mann-Whitney U test. Logistic regression analysis was performed to assess the strength of association of an individual risk factor. Significance was taken as two tailed $p < 0.05$.

Results: There was equal number of patients divided in case and control group. In all 65 males and 35 females and, 59 males and 41 females in case and control group respectively ($p = 0.47$). The distribution of cardiovascular risk factors was significantly ($p < 0.05$; BMI: 23.96 ± 4.37 vs 22.65 ± 4.55 ; diabetes: 10% vs 2%; hypertension: 41% vs 11%; Smoking: 11% vs 1%) higher in CAD patients as compared to control population. The level of HDL was significantly lower in cases, whereas all other lipid parameters except LDL were higher in cases as compared to control ($p < 0.05$). Odds ratio analysis showed that low HDL levels 11.76 (95% CI 4.69 to 29.49) is the strongest associate of CAD amongst all other lipids in Western Indian population.

Conclusion: The study results conclude that in young CAD patients from western India the role of low HDL is significant as compared to other dyslipidemias.

Keywords: Case-control study, Cardiovascular diseases, Dyslipidemias

INTRODUCTION

Coronary Artery Disease (CAD) has become one of the prime health concern in developing countries like India [1]. Asian Indian population have a higher rate of CAD than other ethnic groups and their arteries are almost a decade older than their chronological age [2]. Apart from this Asian Indians are also known to possess different cardiovascular risk factors unique to the population [3]. This disease is often associated with the presence of various risk factors such as elevated blood sugar, blood pressure, dyslipidemia, smoking and obesity.

Dyslipidemia is a cluster of disorder recognized by altered level of TC, TG, LDL, HDL, or TC/HDL ratio. Research has suggested that lipid fractions such as LDL, HDL, TG are associated with cardiovascular disease risk [4]. Current evidence suggests that amongst various dyslipidemias, Asians are highly affected by low HDL levels. Moreover the HDL particle found in this community are relatively small, dense and dysfunctional which are less efficient in reverse cholesterol transport and less protective against CAD [5]. In this study we aimed to study the relation of various dyslipidemias with CAD events in young western Indians. We also wanted to compare the strength of

association of conventional lipid markers with CAD specifically related to this ethnic group.

MATERIALS AND METHODS

This prospective, case-control study was conducted between the period of January 2013 and October 2014 in U. N. Mehta Institute of Cardiology and Research Center, Gujarat, India. The study was approved and cleared by institutional ethics committee. For the study 200 subjects (<40 years of age) were enrolled and divided into two groups:

Group 1 - 100 consecutive patients of CAD with unstable angina/NSTEMI, acute myocardial infarction (STEMI) and of chronic stable angina who were referred for coronary angiography were enrolled.

Group 2 – 100 healthy subjects without any major illness and normal lipid profile were enrolled as control.

Fasting blood sample was collected from the antecubital vein of the subjects under sterile conditions after overnight fasting before blood investigations. Lipid profile parameters such as - TC, TG, TL, lipoproteins (LDL, HDL), VLDL, Lipoprotein (a) were measured by International Federation of Clinical Chemistry (IFCC) approved enzymatic methods using commercially available kit on auto analyser (ARCHITECH PLUS ci4100, Germany) [6]. Lipids levels were classified according to the classification recommended by National Cholesterol Education Program (NCEP) and Adult Treatment Panel III (ATP III) guidelines.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS software v 20.0 (Chicago, IL, USA) Quantitative variables were expressed as mean±standard deviation whereas, qualitative variables were expressed as percentage (%). Comparison between normally distributed data was performed using student's t-test, whereas non-normally distributed data was assessed using Mann-Whitney U-test. Logistic regression analysis was performed to assess the strength of association of an individual risk factor. Level of significance was accepted as $p < 0.05$.

RESULTS

Demographic and clinical profile of the study population – cases and control is presented in [Table/Fig-1]. Both the groups were matched for age and sex as indicated by non-significant difference ($p > 0.05$). The distribution of cardiovascular risk factors was significantly ($p < 0.05$); BMI: 23.96±4.37 vs 22.65±4.55; diabetes: 10% vs 2%; hypertension: 41% vs 11%; smoking habit: 11% vs 1% higher in CAD patients as compared to control population.

The comparison of lipid profile of cases and control population is tabulated in [Table/Fig-2]. The levels of TC (169.28±31.77 vs 143.56±40.25), TG (135.65±75.3 vs 97.13±44.30), non-HDL

cholesterol (137.45±33.68 vs 98.33±41.89), VLDL cholesterol (27.32±15.19 vs 19.43±8.86), LDL/HDL ratio (3.01±1.40 vs 2.45±0.87), TC/HDL (5.01±1.57 vs 3.37±1.36) and Lp (a) (35.13±29.6 vs 26.08±23.91) were significantly ($p < 0.05$) higher in cardiac patients as compared to healthy population. The level of LDL was comparable in both the groups ($p > 0.05$). Whereas, a low HDL level was found in cases (31.83±10.95) as compared to control (45.23±10.19).

The strength of association of individual risk factor in the CAD was estimated with the help of multivariate logistic regression and is described in [Table/Fig-3]. It showed that CAD was highly associated with low HDL 11.76 (95% CI 4.69 to 29.49), followed by elevated TG 3.5 (95% CI 1.22 to 10.03) and TC/HDL 3.38 (95% CI 1.4 to 8.09).

DISCUSSION

Dyslipidemia and its association with CAD events has been reported by many and it is emerging as a major public

Parameters	Cases n=100	Control n=100	p-value
Age	33.73±7.02	33.2±7.6	0.61
Sex (Male/Female)	65/35	59/41	0.47
BMI (kg/m ²)	23.96±4.37	22.65±4.55	0.04
DM-II	10(10)	2(2)	0.03
HTN	41(41)	11(11)	0.002
Smoking	11(11)	1(1)	0.004
CAD	100(100)		
UA/NSTEMI	15(7.5)		
STEMI	75(37.5)		
EA	10(5)		

[Table/Fig-1]: Baseline clinical characteristics and lipid profile of patients and controls.

Values are express as mean±SD and other number (%), BMI: Body mass index, DM-II: Diabetes mellitus-II, HTN: Hypertension, CAD: Coronary artery disease, UA/NSTEMI: Unstable angina/non-ST elevation myocardial infarction, STEMI: ST elevation myocardial infarction, EA: Effort angina. Level of significance accepted $p < 0.05$

Total cholesterol			
Mean±SD	169.28±31.77	143.56±40.25	<0.001
Median	166.00	140.00	
Range	150-189	110.44-171.25	
Triglyceride			
Mean±SD	135.65±75.30	97.13±44.30	<0.001
Median	128.5	86.50	
Range	76.25-161.25	68.25-118	
HDL			
Mean±SD	31.83±10.95	45.23±10.19	<0.001
Median	30.5	44.50	
Range	25.25	36.00	

Non-HDL			
Mean±SD	137.45±33.68	98.33±41.89	<0.001
Median	134	92.50	
Range	116.5-160.0	66.0-126.4	
LDL			
Mean±SD	96.19±42.17	105.52±28.79	<0.001
Median	80.5	102.10	
Range	61.1-112.05	86.6-121.95	
VLDL			
	27.32±15.19	19.43±8.86	<0.001
Median	25.7	17.30	
Range	15.25-33.0	13.65-23.60	
LDL/HDL			
Mean±SD	3.01±1.40	2.45±0.87	<0.001
Median	2.82	2.27	
Range	2.06-3.76	1.84-3.0	
TC/HDL			
Mean±SD	5.01±1.57	3.37±1.36	<0.001
Median	4.65	3.13	
Range	3.83-5.93	2.43-4.03	
Total Lipid			
Mean±SD	616.87±103.12	595.17±83.99	<0.001
Median	601	596.50	
Range	534-675.5	552.75-638.25	
Lipoprotein(a)			
Mean±SD	35.13±29.60	26.08±23.91	<0.001
Median	20.95	16.55	
Range	12.73-59.33	11.45-31.53	

[Table/Fig-2]: The comparison of lipid profile of cases and control population.

Values are express as mean±SD, median and range; HDLC: High density lipoprotein cholesterol, Non-HDL-C cholesterol: Non-high density lipoprotein cholesterol, LDLC: Low density lipoprotein cholesterol, VLDL: Very low density lipoprotein, LDLC/HDL: Low density lipoprotein cholesterol/ High density lipoprotein cholesterol, TC/HDL: Total cholesterol/ High density lipoprotein cholesterol, TL: Total lipid, Lp (a): Lipoprotein (a). Level of significance accepted p=<0.05

health concern in Asian Indians [7]. In majority of these studies, LDL is suggested to play the prime role due to its atherogenic properties. However, the population from Indian subcontinent is known to possess high TG and Lp(a) level along with low HDL levels [8]. This suggests that people from Asian Indian origin are genetically more prone to develop hypertriglyceridemia and hypo high density lipoproteinemia and not the hyper low density lipoproteinemia. In spite of this distinct dyslipidemia pattern of Asian CAD patients, very few studies have reported the prevalence and association of particular lipid abnormalities in various Indian communities.

Low HDL-C is two times more common among Asian Indian men and three times more common among Asian Indian women compared with whites [9]. Several reports have published that in comparison to other ethnic group, the mean HDL levels of Asian Indians is 5 – 15 mg/dL lower [10]. Low HDL-C is a strong predictor of severity of CAD, including left main and three-vessel disease, as well as premature MI and stroke [11-14]. The anti-atherogenic properties of HDL is majorly due to a process known as “cholesterol clearance” also recognised as “reverse cholesterol transport” [15]. However, in recent years the other mechanism of HDL action such as – anti-inflammatory, antioxidative, anti-apoptotic and anti-thrombotic are gaining a lot of attention [16-19]. On the contrary to other dyslipidemic drugs, the strategies for HDL level increase are not established yet [15]. Recently, it has been proposed by many that apart from overall HDL number its functionality is also an important factor for CAD risk [20].

Our study results are in concordance with other reports stating that the prevalence of various dyslipidemia was significantly higher in CAD patients and were contributor of CAD development as indicated by odds ratio analysis [21,22]. However, the key finding of the study was the strongest association of low HDL levels (OR: 11.757; 95% CI – 4.687 – 29.49) with CAD amongst all the reported lipid abnormalities. Other significant contributors were elevated TG, TC/HDL ratio and Lp (a).

The community based epidemiology are often needed to

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
TC	-0.265	0.572	0.214	1	0.644	0.768	0.250	2.354
TG	1.253	0.537	5.443	1	0.020	3.500	1.222	10.025
HDL	2.464	0.469	27.591	1	0.000	11.757	4.687	29.490
TC/HDL	1.216	0.446	7.441	1	0.006	3.375	1.408	8.088
Lp(a)	0.836	0.414	4.071	1	0.044	2.307	1.024	5.196
Constant	-2.029	0.347	34.132	1	0.000	0.132		

[Table/Fig-3]: Odds ratio analysis.

TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein cholesterol, TC/HDL: Total cholesterol/ High density lipoprotein cholesterol, TL: Total lipid, Lp (a): Lipoprotein (a). Level of significance accepted p=<0.05

estimate the ethnic variations in risk factor prevalence. The characteristic dyslipidemia seen in Asian Indians is higher levels of TG, lower HDL levels, and higher levels of Lp(a) [23-25]. As published in our earlier reports, low HDL level (36.53%) was highly prevalent in young healthy Gujarati Indians compared to other dyslipidemia [8]. Similarly, in current study also, we have observed that amongst all the other dyslipidemias, prevalence and strength of hypo-high-density lipoproteinemia in Gujarati CAD patients is highest. The study findings contribute in the current knowledge of racial variation in risk factor distribution and re-emphasise a need for interventions to improve HDL levels in Gujarati Indians.

LIMITATION

The study suffers from two limitations: 1) The sample size of the study is relatively smaller and higher number of patients could be enrolled to obtain association of various other cardiovascular risk factors. 2) This is a single centre study where data was collected from only one region of the state. Involvement of various other centres may have provided more diverse patient pool and in depth evaluation of risk factor profile.

CONCLUSION

This community based case-control study in young western Indian CAD patients shows that low HDL level is the strongest predictor of CAD as compared to all other dyslipidemia. Hence, in order to frame optimal preventive and management strategies for this ethnic group, HDL levels should be closely monitored and controlled by life style interventions or drugs.

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FINANCIAL OR OTHER COMPETING INTERESTS:

None.

Date of Publishing: **Oct 01, 2016**