

## Research Article

# Role of lipid profile in proven premature coronary artery disease and its first degree relatives- a tertiary care hospital based study in South-Eastern region of Rajasthan, India

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## ABSTRACT

**Background:** Cardiovascular diseases have become a leading cause of morbidity and mortality in adult population of Indian sub-continent. Aim of the study was to compare the serum lipid patterns in patients with proven premature CAD and its first degree relative in a tertiary care hospital of South-eastern region of Rajasthan, India.

**Methods:** 200 patients with the primary diagnosis of premature coronary artery disease were enrolled. These patients and their 643 first-degree relatives, who were in the coronary age group 25 years and above also enrolled for the purpose of the study. Fasting lipid profile was estimated.

**Results:** 36.5% of the males and 4.5% female patients were having abnormal cholesterol levels. 30.5 % of male of premature CAD were having high LDL levels as compared to only 2.5% of the females ( $p < 0.05$ ). High LDL level was 33.0%. Low HDL cholesterol in CAD patients were in 36.0% of males and 4.0% of the females ( $p < 0.05$ ). High Triglyceride levels (53.5%) in the CAD patients were 46.5% males and 6.5% females. ( $p < 0.05$ ). Irrespective of sex, majority of relatives (70.7%) were having desirable total cholesterol levels while high total cholesterol was there in only 10.1% of the relatives. 21.4% of male relatives of CAD patients were having abnormal LDL levels as compared to 7.4% of the females ( $p < 0.05$ ).

**Conclusions:** For hyper cholestolaemia, routine screening of all adults older than 20 years is recommended. Therapeutic targets for lipid levels are recommended depending on overall risk for patients with CAD or a CAD risk equivalent such as diabetes or peripheral arterial disease.

**Keywords:** Lipid profile, Coronary artery disease, Cholesterol, HDL

## INTRODUCTION

Cardiovascular diseases have become a leading cause of morbidity and mortality in adult population of Indian sub-continent. The prevalence of coronary artery disease (CAD) has doubled in both rural and urban Indians during the last 20 years.<sup>1</sup> The CAD prevalence in urban India is now fourfold higher than in the US. Although the present high burden of cardiovascular disease deaths is in

itself an adequate reason for attention, a greater cause for concern is the highly malignant form of CAD occurring at an early age in South East Asians.

In contrast to the developed market economies where CAD mortality rates are declining, the mortality rates are accelerating in most developing countries.<sup>2</sup> It has been estimated that 5.3 million deaths attributable to CAD occurred in developing countries in 1990.<sup>3</sup> The

prevalence of conventional risk factors such as smoking, hypertension, and diabetes mellitus in Indians is the same as in other ethnic groups, lipid patterns, however, vary with dietary habits.

South Asians are noted to have higher triglyceride (TG) levels, low concentration of high-density lipoprotein (HDL) cholesterol, increased visceral fat, higher insulin resistance as well as lower total cholesterol (TC) as compared to their western counterparts.<sup>4-10</sup>

The Coronary Artery Disease in Indians (CADI) study has shown that LDL levels do not differ among Asian Indians with or without CAD.<sup>11</sup> The same study has shown abnormally low levels of HDL cholesterol in Indians.

The causal association between lipid levels and cardiovascular diseases risk is indisputable. Low levels of high-density lipoproteins and elevated triglycerides are also clearly associated with excess risk of cardiovascular diseases, and this association holds across racial and ethnic divisions.

The lipid profile appears to have a greater impact on coronary artery disease than on stroke. Worldwide, high cholesterol levels are estimated to cause 56% of global ischemic heart disease and 18% of strokes amounting to 4.4 million deaths annually.<sup>12</sup>

In a hospital-based study from Chennai, 75% patients with myocardial infarction had plasma cholesterol levels less than 200mg/dl. Levels of plasma cholesterol even lower than 150mg/dl has been reported among Indians with coronary artery disease.<sup>13</sup>

The plasma cholesterol levels among the expatriate Indians with coronary artery disease living in UK have been found to be lower as compared to that in the natives.<sup>14</sup>

Elevated serum cholesterol is causally associated with increased risk of CAD. Specifically a 10% increase in serum cholesterol is associated with a 20-30% increase in risk for CAD, and elevations earlier in life may be associated with higher increases in risk.<sup>15</sup>

A recent compilation of three major observational studies underscored the importance of cholesterol levels in the young adult hood to long-term cardiovascular risk, thus substantial evidence suggests that the burden of risk for cardiovascular disease begins in young adulthood.<sup>16</sup>

Because drug therapy will almost certainly prove neither cost effective nor medically appropriate in primary prevention in younger population, intensive life style modification to reduce coronary risk due to lipid disorders should become a social priority. There is insufficient data on lipid levels from India in patients with CAD; only a few studies have been performed in

north India.<sup>17</sup> Therefore the present study was planned to evaluate the role of lipid profile in cad patients and its first degree relatives.

## METHODS

This study was conducted in the Department of medicine, New Medical College Hospital, Kota, Rajasthan from October 2015 to March 2016.

For the purpose of study, 200 consecutive patients admitted in the medical ward /ICU of NMCH, Kota, Rajasthan, India with the primary diagnosis of premature coronary artery disease was enrolled.

These patients and their 643 first-degree relatives, who were in the coronary age group 25 years and above, residing within Kota city or nearby were enrolled for the purpose of the study.

Premature CAD is defined as “sudden death or definite myocardial infarction in male before 55 years of age or in the female before 65 years of age”.<sup>18</sup> Patients with hypothyroidism, nephrotic syndrome, end-stage renal disease, and those receiving hormonal therapy having adverse effect on lipid profile, were excluded from the study.

A written informed consent was taken from each case included in the study after through proper counseling. During 1<sup>st</sup> visit, a detailed history and complete general & systemic examination was done for cases recruited in the study as per Performa.

Blood samples were analyzed for complete lipid profile after 8 hours fasting. During 2<sup>nd</sup> visit, the patients and their relatives were contacted at their homes. They were instructed to go to the standardized laboratory to give the blood samples for lipid profile, after fasting for 10 hours.

At this stage clinical examination of the relatives of the patients were taken. During 3<sup>rd</sup> contact, the study subjects were contacted again and reports of investigations were also handed over to them.

In case any abnormality was detected in the first-degree relatives they were referred for specialty treatment. Statistical analysis was performed with the statistical package for the social science system version SPSS 17.

Continuous variables are presented as mean±SD, and categorical variables are presented as absolute numbers and percentage. Nominal categorical data between the groups were compared using Chi-squared test. P-Value <0.05 was considered statistically significance.

Hyperlipidemia was diagnosed using the criteria described by the Adult Treatment Panel III (ATP III), of U.S. National Cholesterol Education Programme.<sup>19</sup> The cutoff values described were as follows:

**Table 1: The cut off values of hyperlipidemia by adult treatment panel III (ATP III).<sup>19</sup>**

Total cholesterol		LDL cholesterol	
Category	Levels (mg/dl)	Category	Levels (mg/dl)
Desirable	<200	Optimal	<100
Borderline high	200-239	Near optimal	100-129
		Borderline high	130-159
High	240 or above	High	160-189
		Very High	190 or above
HDL cholesterol		Triglyceride	
Category	Levels (g/dl)	Category	Levels (mg/dl)
Low	<40	Normal	<150
Normal	40-59	Borderline	150-199
High	>60	High	200-499
		Very high	>500

**RESULTS**

In this study 87% of the patients suffering from Premature CAD were males. Females represented only 13% of the study population (Table 2).

**Table 2: Distribution of CAD patients according to age and sex.**

Age (years)	Sex				Total	
	Male		Female		No	%
	No	%	No	%		
26-30	12	6.0	0	0.0	12	6.0
31-35	20	10.0	3	1.5	23	10.5
36-40	47	23.5	5	2.5	52	26.0
41-45	81	40.5	18	9.0	99	49.5
46-50	5	2.5	0	0.0	5	2.5
51-55	5	2.5	0	0.0	5	2.5
56-60	4	2.0	0	0.0	4	2.0
Total	174	87.0	26	13.0	200	100.0

**Table 3: Distribution of relatives of CAD patients according to age and sex.**

Age (years)	Sex				Total	
	Male		Female		No	%
	N	%	N	%		
25	12	1.9	3	0.4	15	2.3
26-30	33	5.0	11	1.6	44	6.9
31-35	42	6.3	14	2.1	56	8.7
36-40	59	8.7	26	3.0	85	13.2
41-45	62	9.3	21	3.1	83	13.0
46-50	74	11.1	30	4.5	104	16.2
51-55	30	4.5	17	2.5	47	7.3
56-60	19	2.8	28	4.2	47	7.3
61-65	32	4.8	27	4.0	59	9.2
66-70	31	4.7	20	3.0	51	7.9
70 >	30	4.6	20	3.0	50	7.8
Total	426	66.9	217	33.1	643	100.0

**Table 4: Distribution of CAD patients and its first-degree relatives according to total.**

Category	CAD patients						First degree relative of CAD patients					
	Sex		Sex		Total		Sex		Sex		Total	
	Male		Female		No	%	Male		Female		No	%
	No	(%)	No	(%)			No	(%)	No	(%)		
Desirable	101	(50.5)	17	(8.5)	118	(59.0)	296	(44.4)	161	(24.3)	455	(70.7)
Borderline	39	(19.5)	6	(3.0)	45	(22.5)	87	(13.2)	36	(6.0)	123	(19.1)
High	34	(17.0)	3	(1.5)	37	(18.5)	45	(6.7)	20	(3.0)	65	(10.1)
Total	174	(87.0)	26	(13.0)	200	(100.0)	426	(66.3)	217	(33.7)	643	(100.0)

Amongst CAD patients significantly more i.e. 41.0% were having abnormal total cholesterol levels (borderline

and high) which in first degree relatives was 29.2% (p<0.05) ( $\chi^2=2.1$  DF=2 p<0.05) (Table 4). 30.5 % of male

CAD patients were having abnormal LDL levels (borderline high, high and very high) as compared to only 2.5% of the females and this difference was found to be statistically significant ( $p < 0.05$ ). 21.4% of male relatives of CAD patients were having abnormal LDL levels (borderline high, high and very high) as compared to 7.4% of the females. On application of  $\chi^2$  test, it was found to be significant ( $p < 0.05$ ). Percentage of high or very high LDL Cholesterol level was significantly more i.e. 15.0% among CAD patients as compared to 9.3% in their first-degree relatives, but the borderline values were similar in both the groups. ( $p < 0.05$ ) ( $\chi^2 = 6.2$  DF=4  $p < 0.05$ ) (Table 5).

Low HDL cholesterol level was present in 40.0% of CAD patients. It was distributed to the extent of 36.0% in the male and 4.0% in the female patients. ( $p < 0.05$ ). Low HDL levels in relatives of CAD patients were 40.5% and significantly more males (26.4%) were having this low HDL levels than females (14.1%). Distribution of Low HDL Cholesterol level was equal among patients of premature CAD and their first-degree relatives (40.0% versus 40.6%) ( $\chi^2 = 8.5$  DF= 2  $p > 0.05$ ) (Table 6).

**Table 5: Distribution of CAD patients and its first-degree relatives according to serum LDL cholesterol level.**

Category	CAD patients						First degree relative of CAD patients					
	Sex				Total		Sex				Total	
	Male		Female				Male		Female			
N	%	N	%	N	%	No	%	No	%	No	%	
Optimal	54	27.0	11	5.5	65	32.5	116	18.0	52	8.0	168	26.1
Near optimal	59	29.5	10	5.0	69	34.5	171	26.5	117	18.1	288	44.7
Borderline-high	34	17.0	4	2.0	36	18.0	94	14.6	33	5.1	127	19.7
High	27	13.5	1	0.5	28	14.0	36	5.5	11	1.7	47	7.3
Very high	4	2.0	0	0.0	4	2.0	9	1.3	4	0.6	13	2.0
Total	174	87.0	26	13.0	200	100.0	426	66.3	217	33.7	643	100.0

$\chi^2 = 2.1$  DF=4  $p < 0.05$ ;  $\chi^2 = 4.3$  DF=4  $p < 0.05$

**Table 6: Distribution of CAD patients and its first-degree relatives according to HDL cholesterol levels.**

Category	CAD Patients						First degree relative of CAD patients					
	Sex				Total		Sex				Total	
	Male		Female				Male		Female			
No	%	No	%	No	%	No	%	No	%	No	%	
Low	72	36.0	8	4.0	80	40.0	170	26.4	91	14.1	261	40.0
Normal	91	45.5	16	8.0	107	53.5	240	37.7	119	18.5	359	55.8
High	11	5.5	2	1.0	13	6.5	16	2.4	7	1.0	23	3.6
Total	174	87.0	26	13.0	200	100.0	426	66.3	217	33.7	643	100.0

$\chi^2 = 4.7$ ; DF=3;  $p < 0.05$ ;  $\chi^2 = 3.3$ ; DF=2;  $p < 0.05$ .

**Table 7: Distribution of CAD patients and its first-degree relatives according to Triglyceride levels.**

Category	CAD Patients						First degree relative of CAD patients					
	Number of subjects				Total		Number of subjects				Total	
	Male		Female				Male		Female			
No	%	No	%	No	%	No	%	No	%	No	%	
Normal	81	40.5	13	6.5	94	47.0	222	34.5	133	20.6	355	55.2
Borderline high	30	15.0	3	1.5	33	16.5	91	14.1	40	6.2	131	20.3
High	58	29.0	10	5.0	68	34.5	108	16.7	43	6.6	151	23.4
Very high	5	2.0	0	0.0	5	2.5	5	0.7	1	0.1	6	0.9
Total	174	87.0	26	13.0	200	100.0	426	66.3	217	33.7	643	100.0

Abnormal Triglyceride levels (borderline high, high and very high) were present in 53.5% of the CAD patients. The proportion among males was 46.5% and among female was 6.5% ( $p < 0.05$ ). High Triglyceride levels were

present in 31.5% of male and 12.9% of the female relatives and the difference was statistically significant ( $p < 0.05$ ). Significantly higher proportion ( $p < 0.05$ ) of the patients were having high or very high levels of Serum

Triglyceride as compared to first-degree relatives (36.5% versus 24.3%), while borderline high levels were approximately equally distributed in the patients and the relatives. (16.5% and 20.3%)  $\chi^2=4.1$ DF=3  $p<0.05$  (Table 7).

## DISCUSSION

During the past 30 years, a large decline in cardiovascular diseases has been experienced in the West and substantial increase has been experienced in developing countries. These trends are expected to continue and the medical, social and economic consequences of CAD will be enormous. A greater cause for concern is the CAD occurring at an early age in Indians. An understanding of the risk factors that lead to development of premature CAD is required to develop strategy for prevention. There were 174 male and 26 female CAD patients.

The mean age was 39.7 years. Females were older to their male counter parts (42.6 vs. 38.6 years). Most of them belonged to 40 to 45 years age group. Dwivedi S et al in their "Study on CAD in young; Here do familial or faulty life style" in East Delhi in the year 2000 reported a mean age of 36.6 years of their patients.<sup>20</sup> Male to female ratio in present study was 6.7: 1; this is in fair agreement with other studies reported on CAD in young patients. Male to female ratio of 8:1 has been reported by Vyas A et al in their cross sectional "study of risk factors in patients with MI" published in Indian Practitioner from Bikaner in 1994.<sup>21</sup> Dwivedi et al in the study titled "CV risk factors in young CHD patients around East Delhi" published in South Asian Journal of Preventive Cardiology reported a male to female ratio of 4.5:1.<sup>22</sup>

Total cholesterol, LDL, HDL cholesterol and Triglycerides were measured in all cases. High levels of total cholesterol were detected in 18.5% of the CAD patients, which is quite similar to 16.9% frequency in a study conducted by Shanker Krishna Swami et al in their angiographic study on patients with CAD.<sup>23</sup> High levels were present in 33.0% of the patients in our study. In a study published in American Journal of Cardiology in 2001, Poulter NR has reported that 30.8% cases of premature CAD had High LDL levels.

Low HDL cholesterol levels were reported in 39.2% cases in the same study, which is again almost the same i.e. 40.5% in our study. Subramnium et al also have reported low HDL levels in 46.6% of their patients of CAD.<sup>24</sup> It was interesting to note that 6.5% patients in our study were having high HDL levels, which was also exactly similar i.e. 6.5% in a study conducted by Sharma S et al from New Delhi in their study conducted in the year 2000 on "CAD in young patients".<sup>22</sup> Hypertriglyceridemia was the other lipid abnormality noted in 37.0% of our cases. Almost similar levels of high levels (22.5%) were demonstrated in a study reported in Lancet by Thompson GR in the year 2002.<sup>25</sup>

## Coronary risk factors in first degree relatives of CAD patients

There were 643 relatives (426 males and 217 females) with a male to female ratio of 1.9:1 Females were older to their male counterparts.(47 VS. 43 years) The mean age was 44.3 years. Most of them belonged to 41 to 55 years age group (42.4%). In comparison with the CAD patients mean age was 5 years more but this mean age of relatives was still within the definition of premature CAD age group hence reflecting the relevance of comparative analysis.

Total cholesterol, LDL, HDL cholesterol and Triglycerides were measured in all cases. 29.0% of the relatives of CAD patients were having high LDL levels. A large study of persons developing premature CAD Allen JK et al (Prevalence of Hypercholesterolemia among siblings of persons with premature CAD; Arch Int Med: 1996) showed that high LDL cholesterol levels, more than 160 mg/dl were present in 38.0% asymptomatic siblings of the patients.<sup>26</sup>

Low HDL level was 40.5% in relatives of CAD patients and significantly more males (26.4%) were having this low HDL levels than females (14.1%). High Triglyceride levels were present in 31.5% of male and 12.9% of the female relatives and the difference was statistically significant ( $p<0.05$ ) High triglyceride levels were observed in 24.3% of the relatives in our study. A 33.0% prevalence of high triglyceride levels has been reported from Haryana by Siwach et al.<sup>27</sup>

## CONCLUSION

For hypercholestaemia, routine screening of all adults older than 20 years is recommended. Therapeutic targets for lipid levels are recommended depending on overall risk for patients with CAD or a CAD risk equivalent such as diabetes or peripheral arterial disease.

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