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# The Familial Clustering of Dyslipidemia in Patients with Coronary Artery Disease with Markedly Elevated LDL Cholesterol – A Hospital Based Study in South Kerala Population

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## ABSTRACT

**Background**
High cholesterol level has both an environmental as well as a genetic component. Our aim was to determine the familial clustering of dyslipidemia by screening the relatives of patients with LDL colesterol ≥190 mg/dl.

**Methods**
We performed a cross sectional study to find out the familial clustering of dyslipidemia. The lipid profile of the relatives was also compared with the normal population. Patients within the age group of 18-80 years were included for the study. Only those patients giving consent were included in the study. Study duration was for a period of one year. Cluster sampling technique was used for the study.

**Results**
Among the 50 patients studied, 31(62%) were males and 19 (38%) were females. All of them had LDL cholesterol ≥190 mg/dl. The mean age was 58.4 ±10.5 years. The mean age of the relatives was 39.1 ±10.6 years. The mean total cholesterol level for the relatives is 215±36.7. The mean LDL level for the relatives is 135.5±32.9. Total cholesterol was ≥240mg/dL in 18% of the relatives. LDL was in ≥ 160 mg/dL in 16% of the relatives and in ≥190mg/dL in 10% of the relatives. Total cholesterol and LDL levels are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls ($p<0.01$). Total cholesterol/ HDL ratio was also significantly elevated in relatives of patients compared with normal controls.

**Conclusions**
In our study, total cholesterol, LDL levels and total cholesterol / HDL ratio are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal

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controls ($p < 0.01$).Therefore, cascade screening is strongly recommended in the first degree relatives of patients with markedly elevated LDL cholesterol.
**Keywords-** Dyslipidemia, familial clustering, coronary artery disease, cascade screening.

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in India, accounting for 28% of mortality.[1] Prevalence of CVD in the urban Indian population is between 6.5 to 13.2% and in the rural population between 1.6 to 7.4%. The heavy burden of CVD in Indians is generally considered to be due to increased incidence of metabolic syndrome and an unhealthy lifestyle. Investigations of the genetic causes for this increased trend have been largely unexplored and the contribution of Familial Hypercholesterolemia (FH) is unknown.[1]

High cholesterol level, the major modifiable risk factor for heart disease, has both an environmental as well as a genetic component. LDL cholesterol is well established as a key causal factor in the development of coronary heart disease. Although there is wide variability of LDL cholesterol levels within the population, several studies have demonstrated that LDL cholesterol levels in related individuals tend to be similar, indicating that LDL cholesterol levels is a heritable trait.

Hypercholesterolemia (monogenic and multifactorial) affects 1 in 20 subjects in the general population. On the other hand, frequency of FH is 1 in 500 for heterozygotes and 1 in 1 million for homozygotes. FH is characterized by isolated elevation of plasma low-density lipoprotein cholesterol and is associated with high risk of premature cardiovascular disease. If undiagnosed and untreated, the cumulative risk of CAD by age 60 years is more than 60% among men and 30% among women with heterozygous FH.[2]

There is an urgent need to screen subjects with premature CAD and their relatives in India for the presence of FH, identify the mutations that lead to high cholesterol, and carry out cascade screening in at-risk relatives. Those harbouring mutations in the above genes can be treated to lower the cholesterol levels, prevent early CVD, and avoid death.

## AIMS AND OBJECTIVES

### Primary Objective

To estimate the familial clustering of dyslipidemia in patients with coronary artery disease with markedly elevated LDL cholesterol (LDL C $\geq$ 190 mg/dL).

### Secondary Objective

To compare the lipid profile of relatives with that of normal population.

## MATERIALS & METHODS

The study was a cross sectional study conducted in Government Medical College, Thiruvananthapuram from April 2017 to April 2018. Patients with coronary artery disease who have LDL cholesterol more than or equal to 190 mg/dL were selected. Age of the index case was between 18 and 80 years. Patients with secondary causes of dyslipidemia like hypothyroidism, uncontrolled diabetes mellitus, chronic kidney disease, nephrotic syndrome, clinical features of Cushing′s syndrome and patients on drug therapy like steroids, ART were excluded from the study.

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Informed consent was taken from each patient prior to enrolment into the study. Only patients who give consent for the study was inducted into the study protocol. It was a census type study with all cases during a period of one year. The index cases consecutively registered in OP and IP were taken for the study.

Interview method and a semi structured questionnaire was used. Lab investigations were also used to collect data. Baseline data was collected with proforma including age, gender, symptoms and duration, lipid profile, socio-demographic characteristics and associated diseases and risk factors. LDL cholesterol estimation was done using the indirect method. Familial clustering is the proportion of first degree relatives of the index case (those with LDL cholesterol ≥ 190 mg/dl) who have dyslipidemia.

## STATISTICAL ANALYSIS

Data was collected using proforma and entered into personal computer and analysed using statistical programme, a trial version of Statistics Package for Social Science(SPSS).Quantitative variables were assessed using mean and standard deviation and qualitative variable in proportion. Between group differences of the quantitative variables were evaluated by independent sample test, comparison of quantitative variables among more than two groups were assessed by ANOVA and association of the qualitative variables was analysed by chi- squared test.; Association between quantitative variables was analysed by Pearson correlation. A p-value of<0.05 was considered as the level of significance. Data analysis was performed using SPSS version 17.0.

## RESULTS

The study was conducted from April 2017 through April 2018 in a tertiary care government teaching hospital in Kerala after getting informed consent from each patient .Among the study population of 50 patients majority were between 51 years to 70 years (70%). Maximum age was 74 years and minimum age was 28 years.

Among the study population there were 31 males (62%) and 19 females 8%).In the study population 22% were smokers while 10% were previous smokers who had quit smoking.

Among the study population, inferior wall myocardial infarction (IWMI) was present in 25 (50 %) of the patients, anterior wall myocardial infarction (AWMI) in 18 (36%), lateral wall myocardial infarction (LWMI) in 2 (4%), non ST elevation myocardial infarction (NSTEMI) in 3 (6%), effort angina (EA) in 2(4%).

30% of the study population was diabetic (DM) while 28% of them were hypertensive (HT).History of dyslipidemia (DLP) was present in 28%. History of cerebrovascular accident (CVA) was present in 4% and family history of coronary artery disease (CAD ) was there in 10%.

### Cholesterol level in patients selected for study

94% (47) of the study patients had total cholesterol (≥240mg/dl) . All the patients had LDL cholesterol level ≥ 190mg/dl. HDL levels≥60mg/dl in 4% (2) and 40-59 mg/dl in 44%(22). Triglyceride level < 150mg/dl in 58% (29), 150 -199 mg/dl in 22% (11) and ≥200 mg/dl in 20% (10). The mean and the standard deviations for the same were calculated.

| | Total cholesterol | LDL | HDL | Triglycerides | VLDL |
|---|---|---|---|---|---|

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| | | | | | |
|---|---|---|---|---|---|
| Mean | 287.0 | 218.0 | 41.4 | 145.8 | 28.9 |
| SD | 63.7 | 60.4 | 10.4 | 73.9 | 12.6 |
| Median | 268.5 | 196.0 | 39.0 | 131.5 | 26.0 |
| Q1 | 252.8 | 192.0 | 34.8 | 89.0 | 20.0 |
| Q3 | 291.3 | 218.5 | 50.3 | 196.5 | 37.3 |
| Minimum | 231.0 | 190.0 | 23.0 | 50.0 | 10.0 |
| Maximum | 638.0 | 572.0 | 68.0 | 394.0 | 73.0 |
| ***Table 1: Descriptive statistics for selected variables*** | | | | | |

**Cholesterol level in relative of patients selected for study**

In the relative of patients, majority were between 31 to 50 years i.e. 50(42.5%), 16(20%) of them were below 20 years. 14 of them (17.5%) were above 50 years. Among the relatives 67.5% (54) were children. 27.6% (22) were siblings.

**Lipid profile of the relatives**

18.8%(15) of the relative of patients had ≥240 mg/dl total cholesterol level while 51.3%(41) had 200-239 mg/dl and 30%(24) had total cholesterol < 200mg/dl.LDL cholesterol levels were less than 130mg/dl in 40%(32), 130-159 mg/dl in 43.8%(35) and ≥ 160mg/dl in 16.3%(13)l. HDL levels ≥60 mg/dl in 6.3%(5), 40-59mg/dl in 70%(56) and < 40mg/dl in 23.8%(19). Triglyceride levels were < 150mg/dl in 95% (76), 150-199mg/dl in 3.8% (3) and ≥200mg/dl in 1.3%(1).

| LDL (mg/dL) | Count | Percent |
|---|---|---|
| <100 | 10 | 12.5 |
| 100-129 | 17 | 21.25 |
| 130-159 | 40 | 50 |
| 160-189 | 5 | 6.25 |
| ≥190 | 8 | 10 |
| ***Table 2 : LDL Cholesterol level of relatives*** | | |

| Total cholesterol (mg/dL) | Count | Percent |
|---|---|---|
| <180 | 6 | 7.5 |
| 180-200 | 22 | 27.5 |
| 201-240 | 37 | 46.25 |
| >240 | 15 | 18.75 |
| ***Table 3: Total cholesterol level of relatives*** | | |

**Relationship of cholesterol level in patients with their relative**

The mean total cholesterol level for patients is 292.2±78.2 and that of the relatives is 215±36.7. The mean LDL level for patients is 222.3±75.4 and that of the relatives is 135.5±32.9. The mean HDL level for patients is 40.8±10.7 and that of the relatives is 46.6±.9.8. The mean tryglyceride level for patients is 149.4±72.2 and that of the relatives is 92.2.±40.3. The mean VLDL level for patients is 29.2±12.2 and that of the relatives is 27.6±8.8. Total cholesterol and LDL levels are significantly elevated in the relatives of patients with very high LDL cholesterol ($p < 0.01$).

| | Patient | Relative |
|---|---|---|

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| **Mean** | **292.2** | **215.3** |
|---|---|---|
| SD | 78.2 | 36.7 |
| Median | 267.5 | 204.0 |
| Q1 | 252.3 | 198.0 |
| Q3 | 291.0 | 224.0 |
| Minimum | 231.0 | 131.0 |
| Maximum | 638.0 | 322.0 |

***Table 4: Descriptive statistics for total cholesterol in patients with their relative***

| | **Patient** | **Relative** |
|---|---|---|
| Mean | 222.3 | 135.5 |
| SD | 75.4 | 32.9 |
| Median | 196.0 | 136.0 |
| Q1 | 192.0 | 112.0 |
| Q3 | 218.0 | 152.0 |
| Minimum | 190.0 | 80.0 |
| Maximum | 572.0 | 258.0 |

***TABLE 5: Descriptive statistics for LDL cholesterol in patients with their relative***

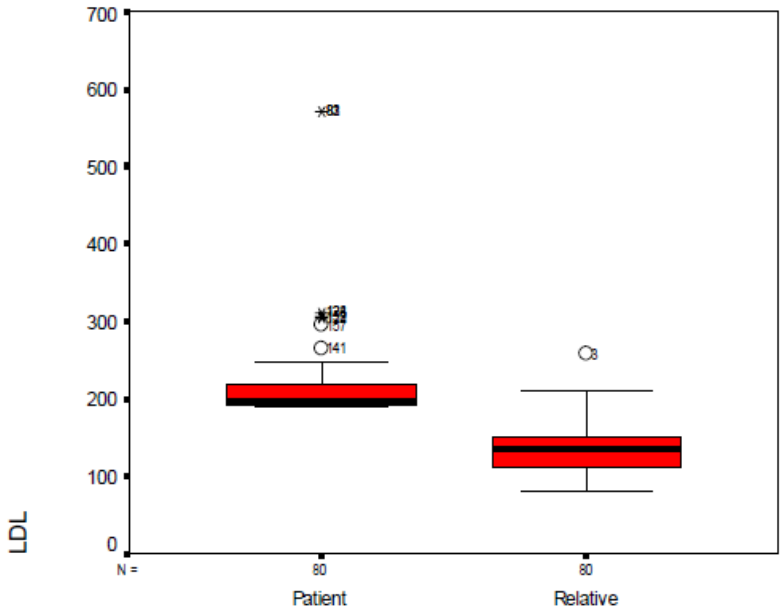


***Fig. 1: Box plot for LDL in patients with their relative***

| | **γ** | **Sig.** |
|---|---|---|
| Total cholesterol | 0.488 | P<0.01 |
| LDL | 0.512 | P<0.01 |
| HDL | -0.116 | 0.303 |
| Triglycerids | -0.112 | 0.323 |

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| | | |
|---|---|---|
| SVLDL | -0.093 | 0.442 |

***Table 6: Correlation of Cholesterol level in patients with their relative***

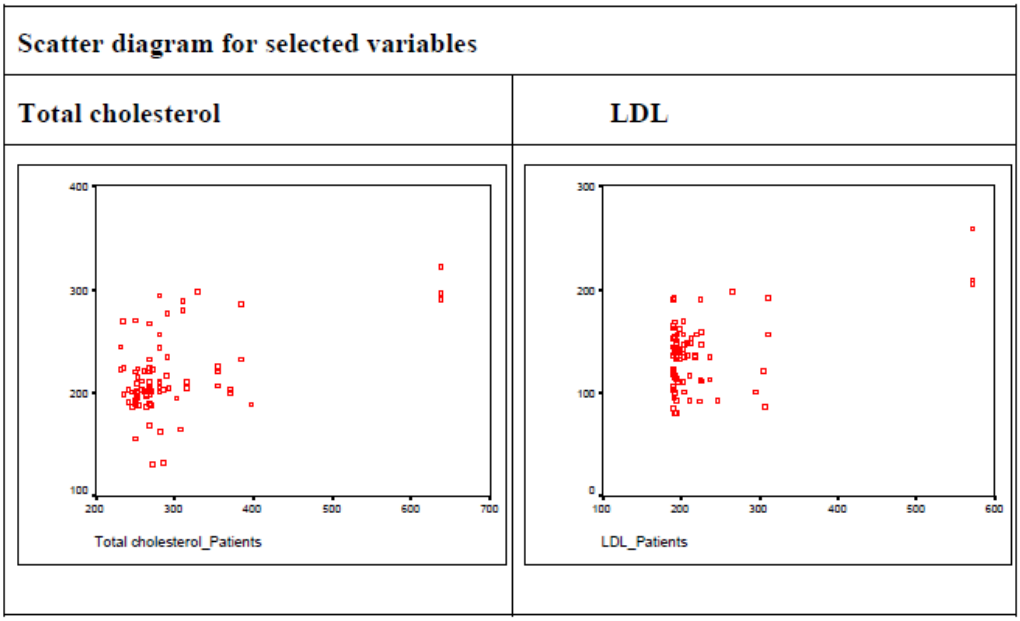


***Fig. 2: Scatter diagram for selected variables***

**Comparison of cholesterol level of relative of patients with normal control**

The mean total cholesterol level for relative of patients is 215.3±36.7 and that of the normal control is191.0±36.6. The mean LDL level for relative of patientsis 135.5±32.9 and that of the normal controlis 98.6±29.2. The mean HDL level for relative of patients is 46.6±9.8 and that of the normal control is 50.4±.11.7. The mean triglyceride level for relatives of patients is 99.2±40.3 and that of normal control is 106.0.±36.0 The mean VLDL level for relatives patients is 27.6±8.8 and that of the normal controls is 25.4±10.8.

Total cholesterol was ≥240mg/dL in 18% of the relatives. LDL was in ≥160 mg/dL) in 16% of the relatives and in ≥190mg/dL in 10%of the relatives.

**Total cholesterol and LDL levels are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls (p< 0.01).**

| | Relative | | | Normal | | | T | p |
|---|---|---|---|---|---|---|---|---|
| | **Mean** | **SD** | **N** | **Mean** | **SD** | **N** | | |
| Total Choleserol | 215.3 | 36.7 | 80 | 191.0 | 36.6 | 100 | 4.42 | P<0.01 |
| LDL | 135.5 | 32.9 | 80 | 98.6 | 29.2 | 100 | 7.96 | P<0.01 |
| HDL | 46.6 | 9.8 | 80 | 50.4 | 11.7 | 100 | 2.29* | 0.023 |
| Triglycerides | 99.2 | 40.3 | 80 | 106.0 | 36.0 | 100 | 1.19 | 0.235 |
| VLDL | 27.6 | 8.8 | 70 | 25.4 | 10.0 | 100 | 1.51 | 0.134 |

*: - Significant at 0.05 level

***Table 7: Comparison of cholesterol level of relative of patients with normal control***

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Total cholesterol/ HDL ratio and LDL/HDL ratio was significantly elevated in relatives of patients compared with normal controls.

| | | Mean | SD | N | t | p |
|---|---|---|---|---|---|---|
| **Total Cholesterol/HDL** | Relative | 4.84 | 1.45 | 80 | 4.75 | P<0.01 |
| | Normal | 3.96 | 1.05 | 100 | | |
| **LDL/HDL** | Relative | 3.04 | 1.03 | 80 | 6.72 | P<0.01 |
| | Normal | 2.09 | 0.88 | 100 | | |

***Table 8: Comparison of cholesterol ratio of relatives of patients with normal control***

## DISCUSSION

Coronary artery disease is a growing problem in India and is a leading cause of death in India. Increased cardiovascular risk may be due to emerging risk factors like metabolic syndrome and glucose intolerance, and also due to hypercholesterolemic conditions like familial hypercholesterolemia.[3-6] Familial hypercholesterolemia may produce 10-20 fold increase in coronary artery disease if not treated properly.[7,8]

India is undergoing a rapid epidemiological transition with increasing population, economic prosperity, urbanization and aging with associated risk factor transition. Increase in cardiovascular risk and hypercholesterolemia is also associated with increase in adverse lifestyles such as greater smoking and tobacco use, change in nutritional habits with greater intake of unhealthy diets and increasing sedentary lifestyle. All have contributed to the rising burden of non-communicable diseases, especially CHD. Even in rural areas of India non-communicable and chronic diseases have become the leading causes for death.[9-11] TheINTERHEART study has reported that apolipoproteins such as high ApoB and low ApoA1 as well as high total and LDL cholesterol are the most important risk factor for CHD globally as well as in South Asian countries.[12-16]

Of plasma-based atherothrombotic risk factors, LDL cholesterol is the best-established risk factor causally linked to incident MI and cardiovascular death. High LDL cholesterol levels consistently predict risk of future cardiovascular events in human populations. Animal studies in multiple species have shown a causal relationship between hypercholesterolemia and atherosclerosis. Abundant evidence provides biologic plausibility for the involvement of LDL in atherogenesis. Furthermore, human mutations that produce hypercholesterolemia on a monogenic basis lead to accelerated atherosclerosis as early as the first decade of life in patients with homozygous familial hypercholesterolemia, while those with heterozygous hypercholesterolemia develop disease approximately 10 to 15 years later. This and other observations have led to the useful office-based concept of a threshold ―cumulative lifetime exposure‖ to LDL cholesterol that, when crossed, results in clinically evident atherosclerosis. Other recently described mutations that affect LDL metabolism, such as those in proprotein convertase subtilisin/kexin type 9 (PCSK9), result in life-long reductions in LDL cholesterol and reduced lifetime risks of events. By contrast, lifetime exposure to moderately elevated levels of LDL cholesterol typically leads to clinical events in the seventh and eighth decades (i.e., 60s and 70s). Finally, interventions in large clinical trials to lower LDL cholesterol levels by various approaches have shown a reduction in cardiovascular events. Thus, LDL cholesterol fulfills the criteria of modified Koch postulates as one causative agent in atherosclerosis.

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Another line of evidence derives from *phylogeny*. Contemporary humans have much higher total and LDL cholesterol levels than those of many other species of higher organisms that thrive nonetheless. Thus, observational, ecologic, and genetic studies suggest that ever lower LDLC levels are likely to confer cardiovascular benefits regardless of starting cholesterol levels for an individual patient.

Cholesterol levels measured early in life influence long-term cardiovascular risk and the burden of risk factors for atherosclerosis, including hypercholesterolemia, and correlate with autopsy-proven fatty streak and raised lesion formation in the arterial tree. Studies with long-term follow-up have suggested that cholesterol levels in youth correlate with long-term risk of MI. Substantial evidence suggests that the burden of risk for CVD begins in young adulthood. Autopsy studies from the Korea and Vietnam conflicts and recent explorations of coronary anatomy by intravascular ultrasonography all indicate that atherosclerosis affects adolescents in Western society, and that this early exposure to elevated levels of LDL cholesterol leads to premature disease in midlife. Visit-to-visit variability in LDL cholesterol is surprisingly wide, and such fluctuations indeed predict subsequent vascular risk.

Hypercholesterolemia is the most common and treatable cause of heart disease. Genetic factors that lead to hypercholesterolemia have not been fully studied in India. Familial Hypercholesterolemia results from mutations in the LDL receptor, ApoB, PCSK9, and ApoE genes. It is imperative to screen subjects with premature CAD and their relatives in India for the presence of FH, identify the mutations that lead to high cholesterol, and carry out cascade screening in the at-risk relatives. Those harbouring mutations in the above genes can be treated to lower the cholesterol levels, prevent early CVD, and avoid death.

In India only limited studies exist on epidemiology of cholesterol and other lipoprotein lipids on large samples in the last 20 years[9-11]. On review of all the recent large population based epidemiological studies that focused on cardiovascular risk factors including cholesterol levels, there were only six multisite studies with sample size ranging from 2000–15,000.[12-17]

Studies that had a large sample size were Indian Industrial Population Surveillance Study (n = 10,442)[12] , India Migration Study (n = 1983)[13] ,Indian Council of Medical Research (ICMR)Integrated Disease Surveillance Project (urban N= 15223, rural N= 13517, slum/periurban N= 15751)[14] , Indian Women Health Study (n = 4624)[15], India Heart Watch (n = 6123)[16], INDIAB study(n = 2042)[17], and a nationwide industry-sponsored Fit Heart Study (n = 46919)[18]. Prevalence of hypercholesterolemia in these studies varies from 10 to 15% in rural to 25–30% in urban populations. These prevalence rates are much lower than in studies from the US and other developed countries. In NHANES studies prevalence of borderline and high cholesterol (≥200 mg/dl) and corresponding borderline and high LDL cholesterol (≥130 mg/dl) varies from 50 to 70% which is much more than in India.[12-17]

In our study, we screened the lipid profile of relatives of patients with markedly elevated LDL cholesterol (≥ 190 mg/dL).The mean total cholesterol level for patients is 292.2 ±78.2 mg/dl and that of the relatives is 215 ±36.7mg/dl. We have also taken the lipid profile of normal population. The mean total cholesterol in the normal control was 191.0±36.6. Total cholesterol was ≥240mg/dL in 18% of the relatives. **Total cholesterol levels are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls (p <0.01).**

In a study utilizing hospital administrative database of more than 67,000 participants prevalence of various dyslipidemias was reported using a fasting sample. In this cohort of mostly middle class men and women there was a high prevalence of various dyslipidemias. Although the most prevalent dyslipidemia in this group was borderline and high LDL

cholesterol(>100 mg/dl), low HDL cholesterol (men 54.9%, women 64.4%) also was highly prevalent.[12]

Another large study (Fit Heart) has reported prevalence of various cholesterol lipoprotein and triglyceride levels in more than 20 states of India utilizing a camp approach to obtain fasting blood samples and uniform laboratory methodology.[18]

This was an industry-sponsored pan-India primary prevention project and used data obtained from lipid evaluation screening camps conducted at 212 locations in urban Indian populations, as part of a primary prevention program conducted during the year 2012. Fasting blood samples from 46,919 subjects aged 18–96 years were obtained. The mean (±1 SD) age was 49.6 ±13.2 years. The pan-India averages (mg/dl) were: total cholesterol 176.7 ± 42.1 mg/dl. There were large inter-state variations in various cholesterol lipoproteins in this study.

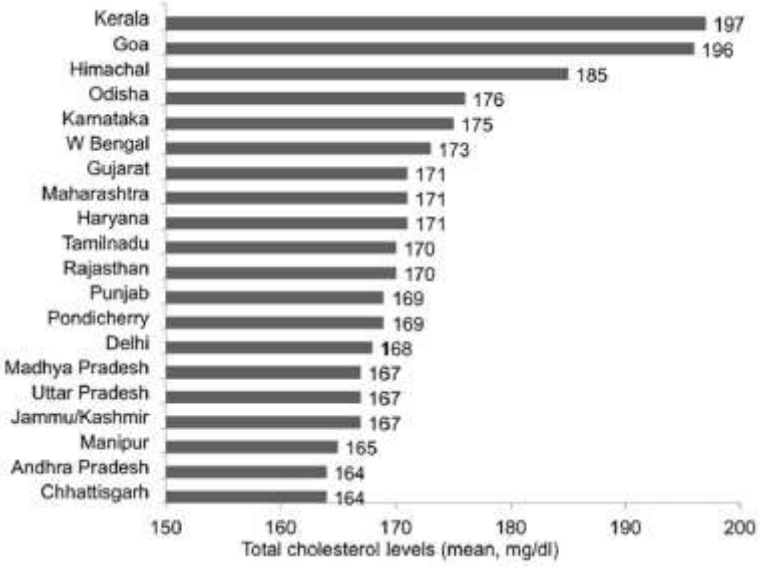


***Fig 3: Mean total cholesterol levels in larger states of India***

In our study, the mean LDL level for relative of patients is 135.5±32.9 mg/dl and that of the normal control is 98.6±29.2 mg/dl. LDL was ≥ 160 mg/dL in 16% of the relatives and in ≥190mg/dL in 10% of the relatives. LDL levels are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls ($p < 0.01$).

Familial hypercholesterolemia is an important coronary risk factor. Its prevalence varies from 1:200 to 1:500 in individuals of Caucasian descent among populations in Europe and North America. Familial hypercholesterolemia is common in individuals who had a myocardial infarction at a young age. As many as one in 200 people could have heterozygous familial hypercholesterolemia, and up to one in 300 000 individuals could be homozygous. The phenotypes of heterozygous and homozygous familial hypercholesterolemia overlap considerably; the response to treatment is also heterogeneous.

The prevalence of suspected familial hypercholesterolemia in India is unknown. To determine prevalence of severe hypercholesterolemia (suspected familial), Rajeev Gupta et al., in their study, evaluated its prevalence in a population-based study and a hospital-based database.[17] In the population-based India Heart Watch, urban middle-class participants in 11 cities in different regions of India were evaluated using cluster sampling. Participants (n = 5350,men 2935, women 2415) were evaluated for demographic, biophysical, and fasting biochemical risk factors.[17] In the hospital-based study, all consecutive fasting blood lipid tests

performed over a seven-year period were analyzed (n = 67347,men 49866, women 17481).[19] The age-adjusted prevalence of severe hypercholesterolemia in population vs hospital based studies was total cholesterol 240–269mg/dl in 5.0% vs 5.5%, 270– 309mg/dl in 2.3% vs 1.8% and ≥310mg/dl in 0.3% vs 0.0.5%. Prevalence of severely high LDL cholesterol in population vs hospital based studies was 160–189mg/dl in 3.6% vs 7.4%, 190–220mg/dl in 1.1% vs 1.7% and ≥220mg/dl in 0.3% vs 0.5% .Severe hypercholesterolemia (LDL cholesterol ≥220mg/dl) in population-based study was 1:357 (men 1:326, women 1:402)and in hospital-based subjects was 1:209 (men 1:271, women1:126). These studies show that although there is a low prevalence of mild to moderate hypercholesterolemia in both population- and hospital-based subjects in India, the prevalence of severe hypercholesterolemia is high and is similar to studies from many high-income countries.

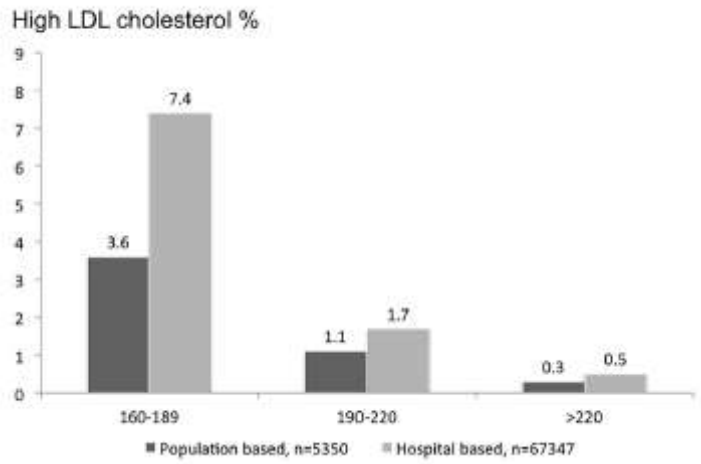


***Fig. 4: Prevalence of severe hypercholesterolemia in population-based and hospital-based cohorts***

In our study, the mean HDL level for patients is 40.8±10.7 and that of the relatives is 46.6±.9.8. The mean HDL level of the normal control is 50.4±.11.7. The mean triglyceride level for patients is 149.4±72.2. The mean triglyceride level for relatives of patients is 99.2±40.3mg/dl and that of normal control is 106.0.±36.0 mg/dl.

Fit Heart study has reported prevalence of various cholesterol lipoprotein and triglyceride levels in more than 20 states of India.[18] . The pan-India averages (mg/dl) were: total cholesterol 176.7 ± 42.1 mg/dl, LDL cholesterol 110.5 ±34.0 mg/dl, HDL cholesterol 43.2 ±11.7 mg/dl, non-HDL cholesterol 133.5 ±41.3 mg/dl and triglycerides 162.3 ± 106.7 mg/dl. Prevalence of various dyslipidemias was also determined. High total cholesterol ≥200 mg/dl was observed in 26.9% (men 24.0%, women 30.8%), LDL cholesterol ≥100 mg/dl in 60.0% (men 57.6%, women 63.1%), HDL cholesterol ≥40/50 mg/dl in men/women in 56.0% (men 49.9%, women 64.5%), non-HDL cholesterol ≥130 mg/dl in 50.8 (men 49.5%, women 52.6%) and triglycerides≥ 150 mg/dl in 42.6% (men 45.6%, women 38.6%).

In our study, total cholesterol was ≥240mg/dL in 18% of the relatives. LDL was in ≥ 160 mg/dL) in 16% of the relatives and in ≥190mg/dL in 10% of the relatives. **Total cholesterol , LDL levels and total cholesterol / HDL ratio are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls (p < 0.01).**

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Special efforts are required to identify individuals with FH in India as they are at high risk of premature coronary heart disease. The condition is seriously underdiagnosed and the diagnosis is often made too late, restricting the benefits of the treatments available. Since this condition is genetically determined, families must become the focus of attention. Cascade testing can identify more individuals with FH who will benefit from early treatment and result in a near-normal life expectancy.

## CONCLUSIONS

Total cholesterol, LDL levels, Total Cholesterol/HDL ratio and LDL/HDL ratio are significantly elevated in the relatives of patients with very high LDL cholesterol compared to normal controls ($p < 0.01$). Cascade screening is strongly recommended in the first degree relatives of patients with markedly elevated LDL cholesterol. Cascade testing can identify more individuals with FH who will benefit from early treatment and result in a near-normal life expectancy. Primary prevention can be initiated at a young age by identifying high risk individuals. With cascade screening many lives can be saved from premature CAD and early death.

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