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Review Article

Recent trends in epidemiology of dyslipidemias in India

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ABSTRACT

Dyslipidemia is the most important atherosclerotic risk factor. Review of population based studies in India shows increasing mean total cholesterol levels. Recent studies have reported that high cholesterol is present in 25–30% of urban and 15–20% rural subjects. This prevalence is lower than high-income countries. The most common dyslipidemia in India are borderline high LDL cholesterol, low HDL cholesterol and high triglycerides. Studies have reported that over a 20-year period total cholesterol, LDL cholesterol and triglyceride levels have increased among urban populations. Case-control studies have reported that there is significant association of coronary events with raised apolipoproteinB, total cholesterol, LDL cholesterol and non-HDL cholesterol and inverse association with high apolipoproteinA and HDL cholesterol. Prevalence of suspected familial hypercholesterolemia in urban subjects varies from 1:125 to 1:450. Only limited studies exist regarding lipid abnormalities in children. There is low awareness, treatment and control of hypercholesterolemia in India.

Contents

1. Prologue

Abnormalities of various cholesterol lipoprotein lipids such as high total cholesterol, low density lipoprotein (LDL) cholesterol, very low density lipoprotein (VLDL) cholesterol and triglycerides and low high density lipoprotein (HDL) cholesterol are important coronary heart disease (CHD) risk factors. There is a strong pathophysiological association of raised LDL cholesterol with initiation and progression of coronary atherosclerosis. Robust data are available that shows that lowering its levels can regress and stabilize atherosclerotic vascular disease. Similar, though not as robust, data are also available for raised triglycerides and low HDL cholesterol.

University of Oxford-based Prospective Studies Collaboration gathered information from 61 prospective observational studies, mostly in Western Europe and North America, consisting of more than 900,000 adults without previous CHD or vascular disease with baseline measurements of total cholesterol and blood pressure.[1] During 12 million person years of follow-up of persons between the ages of 40 and 89 years, there were more than 55,000 vascular deaths (CHD 34,000, stroke 12,000, others 10,000).

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Information regarding HDL cholesterol was available for 150,000 participants, among whom there were 5000 vascular deaths (CHD 3000, stroke 1000, other 1000). It was reported that 39 mg/dl lower total cholesterol was associated with about a half lower IHD mortality (hazard ratio 0.44 [95% CI 0.42–0.48]) at age-group 40–49 years, a third lower IHD mortality (0.66 [0.65–0.68]) at age-group 50–69 years, and a sixth lower CHD mortality (0.83 [0.81–0.85]) at age 70–89 years in both sexes (Fig. 1).[1] This was observed throughout the main range of cholesterol in most developed countries, with no apparent threshold. Of various simple indices involving HDL cholesterol, the ratio total/HDL cholesterol was the strongest predictor of CHD mortality (40% more informative than non-HDL cholesterol and more than twice as informative as total cholesterol).

The Cambridge University based Emerging Risk Factors Collaboration obtained individual records on 302,430 people without initial vascular disease from 68 long-term prospective studies, again, mostly in Europe and North America. [2] During 2.79 million person-years of follow-up, there were 8857 nonfatal myocardial infarctions, 3928 CHD deaths, 2534 ischemic strokes, 513 hemorrhagic strokes, and 2536 unclassified strokes. It was reported that rates of CHD per 1000 person-years in the bottom and top thirds of baseline lipid distributions, respectively, were 2.6 and 6.2 with triglyceride, 6.4 and 2.4 with HDL cholesterol, and 2.3 and 6.7 with non-HDL cholesterol. Adjusted hazard ratios (HRs) for CHD were 0.99 (95% CI, 0.94–1.05) with triglyceride, 0.78 (95% CI, 0.74–0.82) with HDL cholesterol, and 1.50 (95% CI, 1.39–1.61) with non-HDL cholesterol. For the subset with apolipoproteins or directly measured LDL cholesterol, HRs were 1.50 (95% CI, 1.38–1.62) with the ratio non-HDL/HDL cholesterol, 1.49 (95% CI, 1.39–1.60) with the ratio apo B/apo AI, 1.42 (95% CI, 1.06–1.91) with non-HDL cholesterol, and 1.38 (95% CI, 1.09–1.73) with directly measured LDL cholesterol. This study highlighted the importance of LDL cholesterol as well as non-HDL cholesterol.

The Cholesterol Treatment Trialists' Collaboration reported efficacy and safety of LDL lowering therapy among 174,000 men and women who participated in 27 randomized trials.[3] In this study the researchers performed meta-analyses on data from 22 trials of statin therapy versus control (n = 134,537) and five trials of more-intensive versus less-intensive statin therapy (n = 39,612). Effects on major vascular events, major coronary events, stroke, coronary revascularization and mortality were weighted per 38.7 mg/dl (1.0 mmol/L) reduction in LDL cholesterol and effects in men and women compared with a Cox model that adjusted for non-sex differences. The proportional reductions per 38.7 mg/dl reduction in LDL cholesterol in major vascular events were similar overall for women (rate ratio [RR] 0.84, 99% CI 0.78–0.91) and men (RR 0.78, 99% CI 0.75–0.81, adjusted p value for heterogeneity by sex = 0.33) and also for those women and men at less than 10% predicted 5 year absolute cardiovascular risk (adjusted heterogeneity p = 0.11). Likewise, the proportional reductions in major coronary events, coronary revascularization, and stroke did not differ significantly by sex. No adverse effect on rates of cancer incidence or non-cardiovascular mortality was noted for either sex. These net benefits translated into all-cause mortality reductions with statin therapy for both women (RR 0.91, 99% CI 0.84-0.99) and men (RR 0.90, 99% CI 0.86–0.95; adjusted heterogeneity p = 0.43). This study clearly demonstrated efficacy and safety of statin

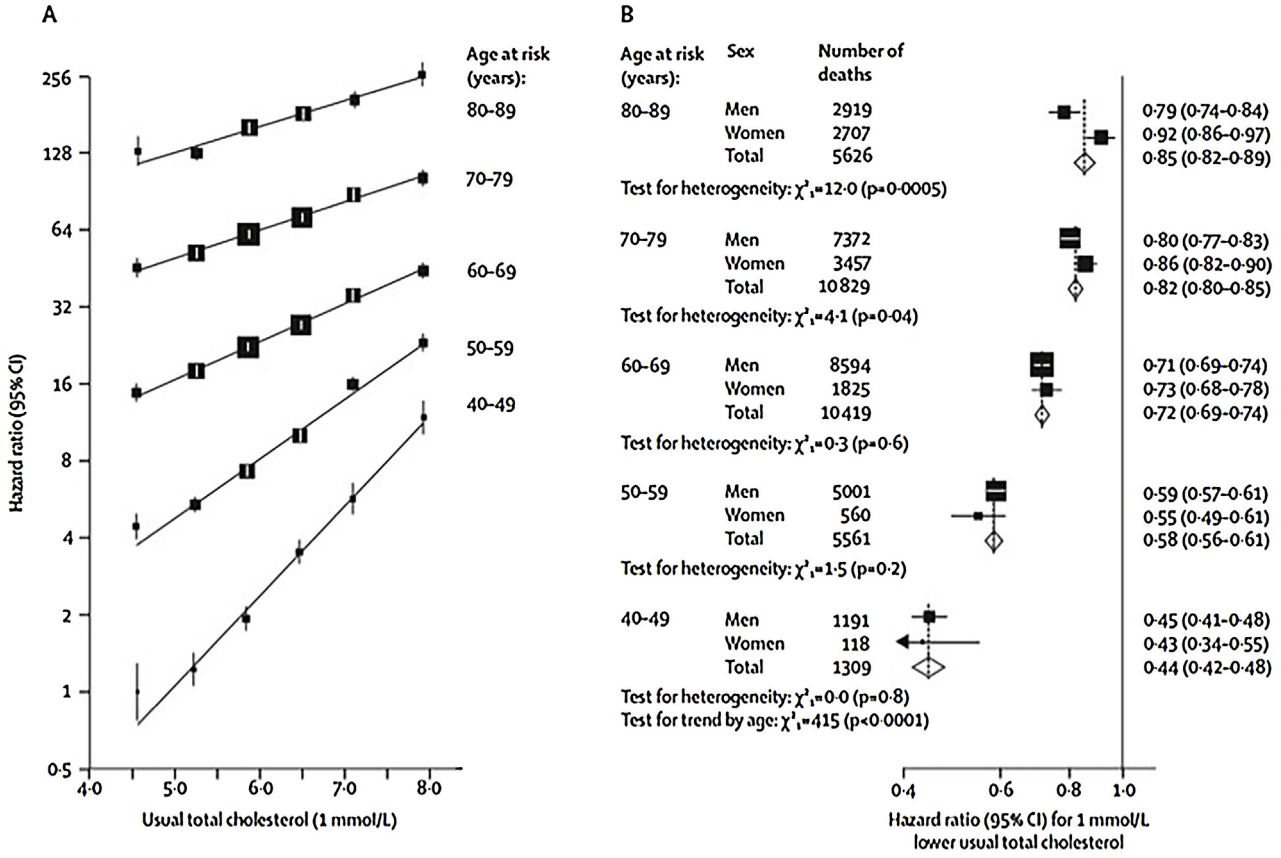

Fig. 1. Total cholesterol and ischemic heart disease mortality in Prospective Studies Collaboration.

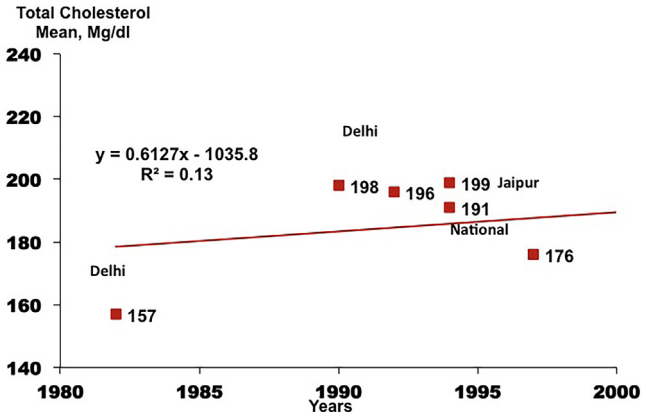

Fig. 2. Increasing mean cholesterol levels in population-based studies in India from 1960s to 1990s.

therapy and, along with many other studies, supported its widespread use in men and women at high risk for coronary events. [4]

Global Burden of Metabolic Risk Factors Study reported trends in total cholesterol levels in different countries and various regions of the world from the years 1980–2008. [5] It was estimated that total cholesterol levels increased in India as well as many other low-income and lower-middle income countries over this period. [6] On the other hand, cholesterol levels declined in most high-income countries.[6] These trends were derived using mathematical modeling from sparse epidemiological studies in a number of countries. Good quality data were available from high-income countries due to periodic nationwide surveys (e.g., USA, UK, Germany, Japan, etc.). On the other hand, in low and lower-middle countries, including India, high quality epidemiological data are not available and trends were determined using probabilistic estimations. [6]

In the present article we have reviewed recent studies of prevalence of dyslipidemias and levels of cholesterol lipoproteins and triglycerides in India. Epidemiological studies of other important cardiovascular risk factors, including determinants of dyslipidemias, such as body mass index and obesity,[7] abdominal obesity and metabolic syndrome [8], blood pressure and hypertension [9,10], diabetes [11,12] and various lifestyle factors[13] have been reviewed recently and are not included in the present report.

2. Indian epidemiological studies

We reviewed prevalence and trends in cholesterol levels in India using studies from 1960′s to 1990′s. [14] Heterogeneous data using different methodologies were available and although there was an increasing secular trend in total cholesterol levels ($R^2 = 0.13$, Fig. 2), in view of various limitations and biases in data, robustness of this trend could not be confirmed.

In India only limited studies exist on epidemiology of cholesterol and other lipoprotein lipids on large samples in the last 20 years[14–16]. We reviewed all the recent large population based epidemiological studies that focused on cardiovascular risk factors including cholesterol levels and found that there were only six multisite studies with sample size ranging from 2000–15,000. [17–22] None of these studies is nationally representative (Table 1). Studies that had a large sample size were Indian Industrial Population Surveillance Study (n = 10,442), [17] India Migration Study (n = 1983), [18] Indian Council of Medical Research (ICMR) Integrated Disease Surveillance Project (urban N = 15223, rural N = 13517, slum/periurban N = 15751), [19] Indian Women Health Study (n = 4624), [20] India Heart Watch (n = 6123), [21] INDIAB study (n = 2042)[22] and a nationwide industry-sponsored FitHeart Study (n = 46919)[23]. Prevalence of hypercholesterolemia in these studies is shown in Table 1 and 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. [5]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. [24]

An important shortcoming of Indian epidemiological studies is lack of large studies with details of patterns of dyslipidemia.[25] When compared with the western populations, Indians and migrant South Asians tend to have higher triglycriede levels and lower HDL cholesterol while total cholesterol levels are lower than in the US and the UK.[26–28] Migrant cross-sectional studies have reported that compared to Caucasians and migrant south Asians, Indians in India have lower total cholesterol and lower HDL cholesterol and greater triglyceride levels.[29,30] Studies from India have also reported greater triglyceride levels in rural and urban populations associated with low HDL cholesterol levels.[31,32] The low HDL cholesterol and hypertriglyceridemia are metabolically interlinked and their combination has been termed as atherogenic dyslipidemia.[33] This is also associated with increased levels of small-dense LDL particles and insulin resistance.[34] Atherogenic dyslipidemia is particularly common in South Asians and has been shown to have a strong association with type 2 diabetes mellitus, metabolic syndrome and CHD.[35] This could be related to high carbohydrate diets in South Asian populations.[36] Prognostic implications of this finding have not been well studied in South Asians or in India.[37]

Only a few large studies have reported prevalence of different forms of lipid abnormalities among Indians. India Heart Watch study was conducted among urban middle class subjects in 11 cities of India with fasting lipid estimation. [21] Prevalence of various

Table 1
Prevalence of hypercholesterolemia (≥200 mg/dl) in multisite Indian studies.

Study and Sites	Year reported	Sample size	Prevalence (%)	
			Men	Women
Indian Industrial Population Surveillance Study: Urban[17]	2006	10,442	25.1	–
India Migration Study: Rural[18]	2010	1983	21.1	27.8
ICMR Integrated Disease Surveillance Project: Urban[19]	2010	15,223	31.7	32.8
ICMR Integrated Disease Surveillance Project: Rural[19]	2010	13,517	19.5	26.4
ICMR Integrated Disease Surveillance Project: Periurban/Urban Slum[19]	2010	15,751	18.1	23.4
Indian Women's Health Study: Urban[20]	2013	2008	–	27.7
Indian Women's Health Study: Rural[20]	2013	2616	–	13.5
India Heart Watch: Urban[21]	2014	6123	25.1	24.9
ICMR INDIAB Study: Rural & Urban[22]	2014	2042	13.9	?
FitHeart Study: Urban[23]	2014	46,919	29.0	30.8

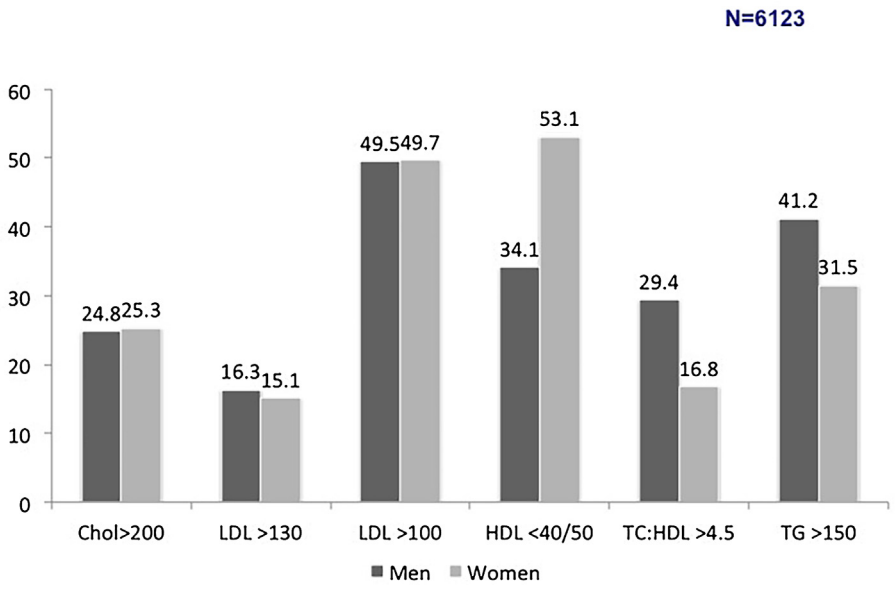

Fig. 3. Prevalence of various dyslipidemias in India Heart Watch multisite study.

cholesterol lipoprotein abnormalities after age-adjustment in men and women, respectively were, total cholesterol ≥200 mg/dl in 25.1% and 24.9%, LDL cholesterol ≥130 mg/dl in 16.3% and 15.1% and ≥ 100 mg/dl in 49.5% and 49.7%, HDL cholesterol <40 mg/dl (men) and <50 mg/dl (women) in 33.6% and 52.8%, total:HDL cholesterol ratio ≥4.5 in 29.4% and 16.8% and triglycerides ≥150 mg/dl in 42.1% and 32.9% (Fig. 3). The prevalence rates of various fasting dyslipidemia in the first phase of ICMR INDIAB study[22] restricted to urban and rural populations in 4 states in India was hypercholesterolemia in 13.9%, high triglycerides in 29.5%, low HDL cholesterol in 72.3% and high LDL cholesterol in 11.8%. 79% men and women had abnormalities in at least one of the lipid parameters.

In a study utilizing hospital administrative database of more than 67,000 participants we reported prevalence of various dyslipidemias using a fasting sample. [38] In this cohort of mostly middle class men and women there was a high prevalence of various dyslipidemias (Fig. 4). 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. Another large study (FitHeart) 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.[23] 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 by a pharmaceutical company 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, LDL cholesterol

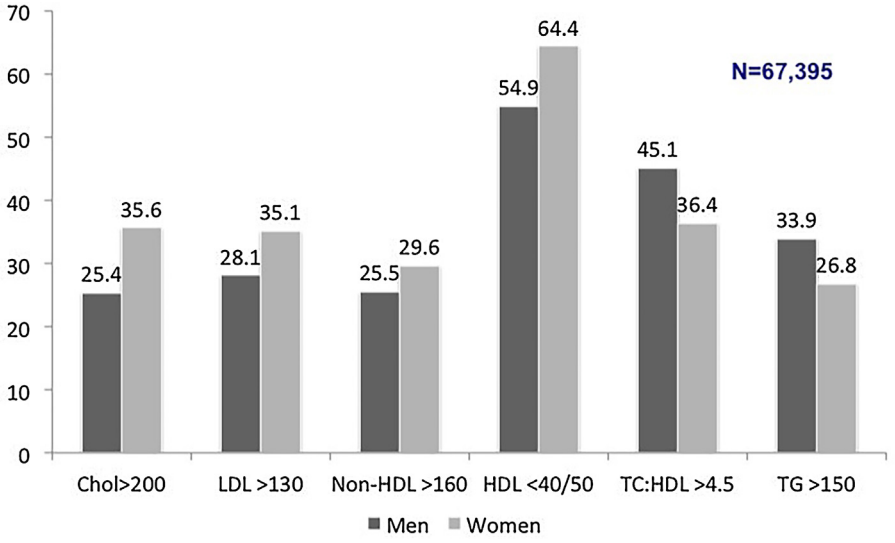

Fig. 4. Prevalence of various dyslipidemias in a large hospital database.

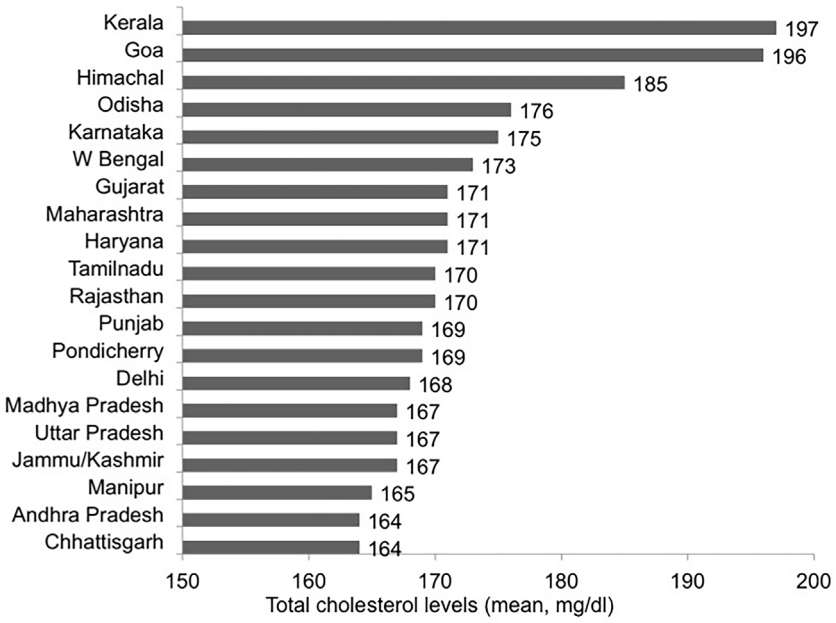

Fig. 5. Mean total cholesterol levels in larger states of India.

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. There were large inter-state variations in various cholesterol lipoproteins in this study (Fig. 5). 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%) (Fig. 6). This study reported large inter-state variation in mean levels of various cholesterol lipoproteins and lipids as well as prevalence of various lipid abnormalities. The prevalence of high total cholesterol varied from 13.8–48.2%, high LDL cholesterol 46.9–82.6%, low HDL cholesterol 42.2–69.4%, high non-HDL cholesterol 38.0–71.8% and high triglycerides 34.2–60.5%. Indian states were divided into tertiles of Human Development Index. There was a significant association of state-level Human Development Index with prevalence of various dyslipidemias (Fig. 7). Better developed states had greater prevalence of cholesterol-related dyslipidemias such as hypercholesterolemia, high LDL cholesterol and high non-HDL cholesterol while states with low Human Development Index had greater prevalence of hypertriglyceridemia. These data are similar to India Heart Watch study which reported similar differences in geographic distribution of lipids and other cardiovascular risk factors. [39]

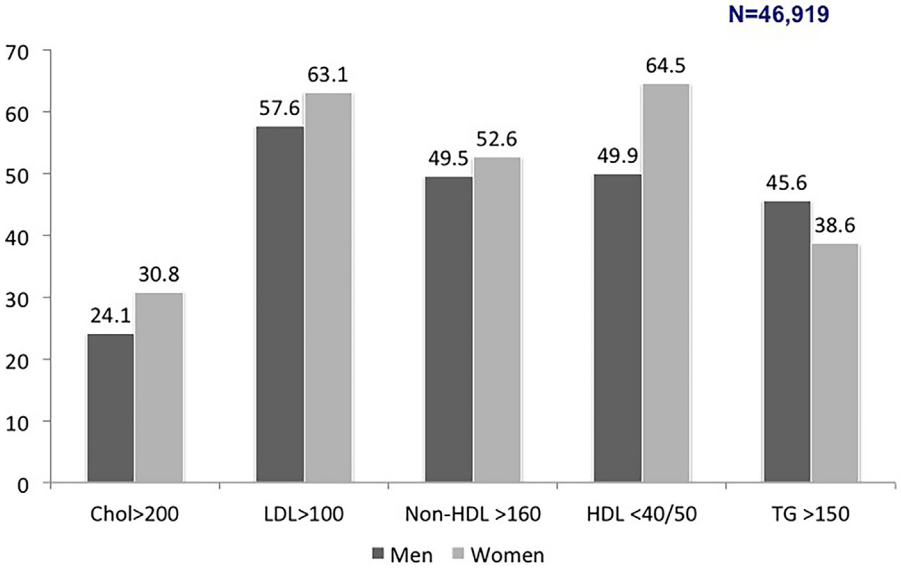

Fig. 6. Prevalence of various dyslipidemias in the multicentric FitHeart Study.

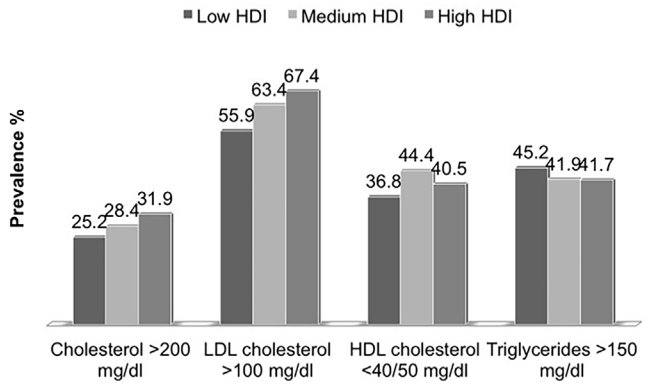

Fig. 7. Association of State-level Human Development Index (HDI) tertiles with prevalence of various dyslipidemias in India.

3. Lipid trends in india

India is undergoing a rapid epidemiological transition with increasing population, economic prosperity, urbanization and aging with associated risk factor transition.[40]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.[41,42] 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.[15] The INTERHEART 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. [43] Trends in these metabolic risk factors have not been well studied.

Jaipur Heart Watch (JHW), a series of cross sectional studies in an Indian urban population, reported secular trends in cholesterol and other lipoproteins over a 20-year period. [32,44] The first review was performed to determine secular trends in prevalence of various lipid abnormalities in an urban Indian population over a 12-year period.[32] Data from successive epidemiological studies performed in Jaipur were analyzed. The studies evaluated adults ≥20 years for multiple coronary risk factors using standardized methodology (JHW-1, 1993-94, n = 2212; JHW-2, 1999–2001, n = 1123; JHW-3, 2002-03, n = 458, and JHW-4 2004–2005, n = 1127). Data of subjects 20–59 years (n = 4136, men 2341, women 1795) were included. In successive studies, fasting measurements for cholesterol lipoproteins (total cholesterol, LDL cholesterol, HDL cholesterol) and triglycerides were performed in 193, 454, 179 and 252 men (n = 1078) and 83, 472, 195, 248 women (n = 998) (total 2076). Trends in age-adjusted prevalence (%) of dyslipidemias in JHW-1, JHW-2, JHW-3 and JHW-4, respectively, showed insignificant changes in high total cholesterol (26.3, 35.1, 25.6, 26.0, R = 0.034), high LDL cholesterol (24.2, 36.2, 31.0, 22.2, R = 0.062), and low HDL cholesterol (46.2, 53.3, 55.4, 33.7, R = 0.136) while increase was observed in prevalence of high non-HDL cholesterol (23.0, 33.5, 27.4, 26.6, R = 0.026), high VLDL cholesterol (40.1, 40.3, 30.1, 60.6, R = 0.143), high total:HDL cholesterol ratio >5.0 (22.2, 47.6, 53.2, 26.3, R = 0.031), and high triglycerides (25.7, 28.2, 17.5, 34.2, R = 0.047). It was concluded that in this cohort the prevalence of subjects with high total cholesterol did not change significantly while those with high non-HDL cholesterol, VLDL cholesterol and triglycerides as well as with high total:HDL cholesterol increased. The study also reported a significant association of increasing dyslipidemias with increasing truncal obesity and obesity.[32]

In the second review of JHW studies, 20-year trends in mean cholesterol and various lipid parameters were evaluated.[44] The number of subjects aged 20–59 years evaluated were 712 in JHW-1, 558 in JHW-2, 374 in JHW-3, 887 in JHW-4, 530 in JHW-5 and 1100 in JHW-6. Across the studies, there was high prevalence of overweight, hypertension, and lipid abnormalities. Age- and sex-adjusted trends showed significant increases in mean body mass index, fasting glucose, total cholesterol, HDL cholesterol and triglycerides (quadratic and log-linear regression, $p < 0.001$).[44] Categorical trends showed increase in overweight and obesity ($p < 0.05$) while insignificant changes were observed in truncal obesity, hypertension, hypercholesterolaemia and diabetes. On the other hand the prevalence of hypertriglyceridemia increased (Fig. 8).

Although there are no studies that evaluated trends in hypercholesterolemia in rural populations, review of previous

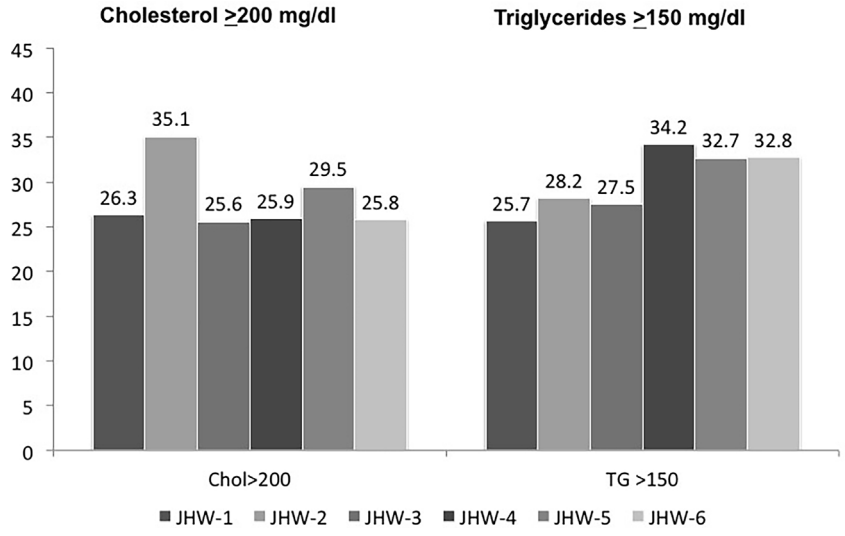

Fig. 8. 20-year trends in prevalence of hypercholesterolemia and hypertriglyceridemia among urban subjects in Jaipur Heart Watch (JHW).

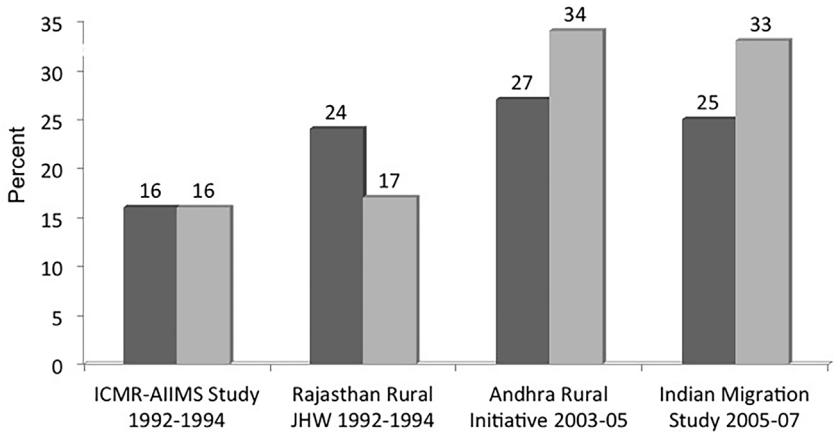

Fig. 9. Increasing prevalence of hypercholesterolemia in rural men and women.

Table 2
Relative risk (95% confidence intervals) for acute myocardial infarction in different ethnic groups for various lipid measures with 1SD change in the INTERHEART study.[43]

	South Asians	European	Chinese	Latin American	Overall
Total cholesterol	1.23 (1.14–1.31)	1.08 (1.02–1.15)	1.16 (1.09–1.23)	1.05 (0.97–1.14)	1.16 (1.13–1.19)
HDL cholesterol	0.97 (0.90–1.05)	0.78 (0.73–0.83)	0.83 (0.78–0.88)	1.03 (0.94–1.13)	0.85 (0.83–0.88)
Non-HDL cholesterol	1.23 (1.15–1.31)	1.17 (1.10–1.24)	1.24 (1.18–1.31)	1.04 (0.96–1.28)	1.21 (1.17–1.24)
Apolipoprotein A-1	0.72 (0.66–0.78)	0.70 (0.66–0.75)	0.67 (0.63–0.71)	0.67 (0.61–0.74)	0.67 (0.65–0.70)
Apolipoprotein B	1.38 (1.29–1.48)	1.24 (1.16–1.32)	1.28 (1.20–1.36)	1.18 (1.09–1.28)	1.32 (1.28–1.36)
Total:HDL cholesterol ratio	1.10 (1.04–1.17)	1.31 (1.21–1.42)	1.34 (1.24–1.45)	0.97 (0.90–1.05)	1.17 (1.13–1.20)
Apo B:ApoA-1 ratio	1.53 (1.42–1.64)	1.47 (1.37–1.59)	1.77 (1.63–1.92)	1.27 (1.17–1.38)	1.59 (1.52–1.64)

studies shows increasing trends in these populations also (Fig. 9). The prevalence of total cholesterol >200 mg/dl in early 1990's was 16%[15] and has increased to 25–35% in more recent Andhra Pradesh Rural Health Initiative and India Migration Study [18].

4. Lipids and heart disease in india

The relative importance of different lipid components in acute coronary syndrome in different ethnic groups has been highlighted in the INTERHEART study (Table 2) [43]. In this study, apolipoprotein A-1 was a better marker of protection (odds ratio, OR, 0.72, CI 0.66–0.78) than HDL cholesterol (OR 0.97, CI 0.90–1.05) while raised apo B:apo A-1 was the best indicator of risk. However, the risk associated with 1 standard deviation change in total cholesterol, non-HDL cholesterol, apolipoprotein B_{100}, total:HDL cholesterol ratio apolipoprotein B_{100}:apolipoprotein A-1 ratio was similar in South Asians to other ethnic groups.

Smaller case-control studies in India have reported strong association of high total cholesterol, low HDL cholesterol and raised triglycerides with CHD or acute myocardial infarction.[14] A large study of case control study of premature CHD in Bikaner, Rajasthan (cases 165, controls 199) used multivariate logistic regression (odds ratio, 95% confidence intervals) to identify risk factors of importance.[45]It was reported that smoking (19.41, 6.82–55.25), hypertension (8.95, 5.42–14.79), high LDL cholesterol (2.49, 1.62–3.84), low HDL cholesterol (10.32, 6.30–16.91), high

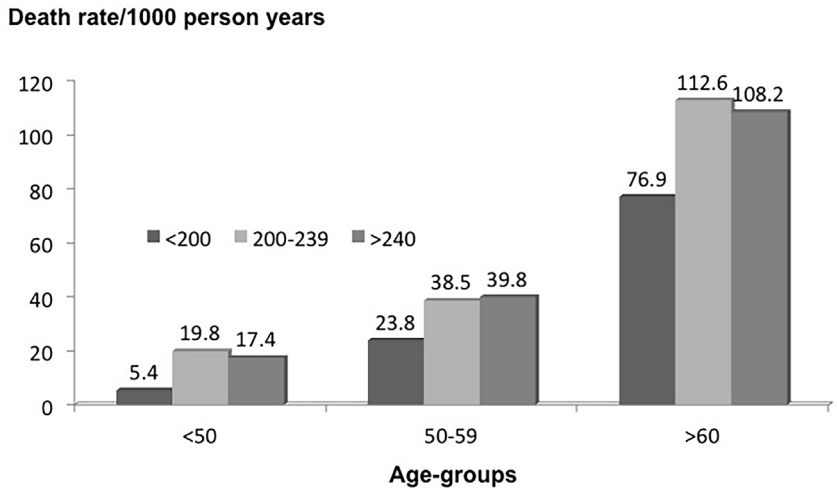

Fig. 10. Prospective study of association of cholesterol levels with cardiovascular mortality in patients with pre-existing CHD.

triglycerides (3.62, 2.35–5.59), high total:HDL cholesterol (3.87, 2.35–5.59), high fibrinogen (2.87, 1.81–4.55) and high homocysteine (10.54, 3.11–35.78) were significant factors.

There are no studies that have prospectively evaluated importance of various cholesterol lipoproteins in India. In a small prospective observational study, 502 patients with pre-existing CHD were evaluated for long-term cardiovascular mortality.[46] The study was performed in the pre-statin era with limited availability of cholesterol lowering medications. It was observed that there was a linear relationship of increasing total cholesterol levels with increasing mortality in various age-groups (Fig. 10). A borderline high total cholesterol (200–239 mg/dl) as well as high total cholesterol (>240 mg/dl) was associated with a greater hazard of mortality at a mean of 5 years of follow-up. Recent studies of this type could all be vitiated with widespread use of statins and we may not be able to obtain similar data in secondary prevention setting.

There are a number of population based epidemiological studies available in India that have evaluated age-related cardiovascular mortality.[47] However, no study has evaluated roles of various cholesterol lipoproteins and triglycerides. The ongoing Prospective Urban Rural Epidemiology (PURE) study can provide some insights into this important question. The first follow-up of this study has reported that there is a strong association of INTERHEART Risk Score with cardiovascular outcomes, globally, as well as in India.[48] Further results are awaited.

5. Severe hypercholesterolemia

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.[49] 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.[49] 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), we evaluated its prevalence in a population-based study and a hospital-based database.[21,38] In the population-based India Heart Watch,[21] we evaluated urban middle-class participants in 11 cities in different regions of India using cluster sampling. Participants (n = 5350, men 2935, women 2415) were evaluated for demographic, biophysical, and fasting biochemical risk factors. 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).[38] The age-adjusted prevalence of severe hypercholesterolemia in population vs hospital based studies was total cholesterol 240–269 mg/dl in 5.0% vs 5.5%, 270–309 mg/dl in 2.3% vs 1.8% and ≥310 mg/dl in 0.3% vs 0.0.5%. Prevalence of severely high LDL cholesterol in population vs hospital based studies was 160–189 mg/dl in 3.6% vs 7.4%, 190–220 mg/dl in 1.1% vs 1.7% and ≥220 mg/dl in 0.3% vs 0.5% (Fig. 11). Severe hypercholesterolemia (LDL cholesterol ≥220 mg/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, women 1:126). 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.[49] Larger studies are required to exactly assess the prevalence of suspected familial hypercholesterolemia in India.

A few genetic studies on identification of DNA patterns and single nucleotide polymorphisms for familial hypercholesterolemia in India have been performed.[50,51] Results of larger registry-based studies are awaited. Studies to identify epigenetic associations of lipid abnormalities with adiposity are also needed. A recent epigenome-wide association study of body mass index and adverse outcomes of adiposity have reported significant disturbances of DNA methylation with type 2 diabetes and in prediction of CHD risk.[52]

6. Hypercholesterolemia in childhood

There is limited information on prevalence of lipid abnormalities and hypercholesterolemia in childhood in India.[37] In a study at Jaipur, 237 school children aged 13–17 years were evaluated using

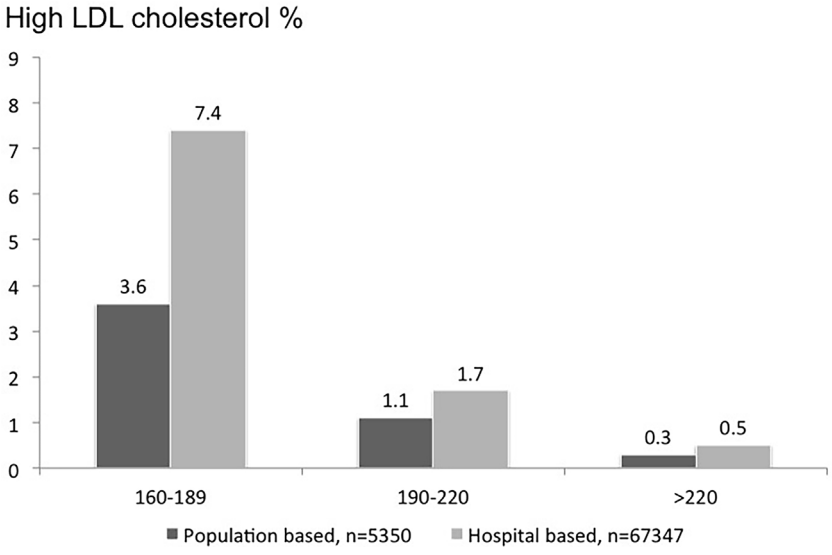

Fig. 11. Prevalence of severe hypercholesterolemia in population-based and hospital-based cohorts.

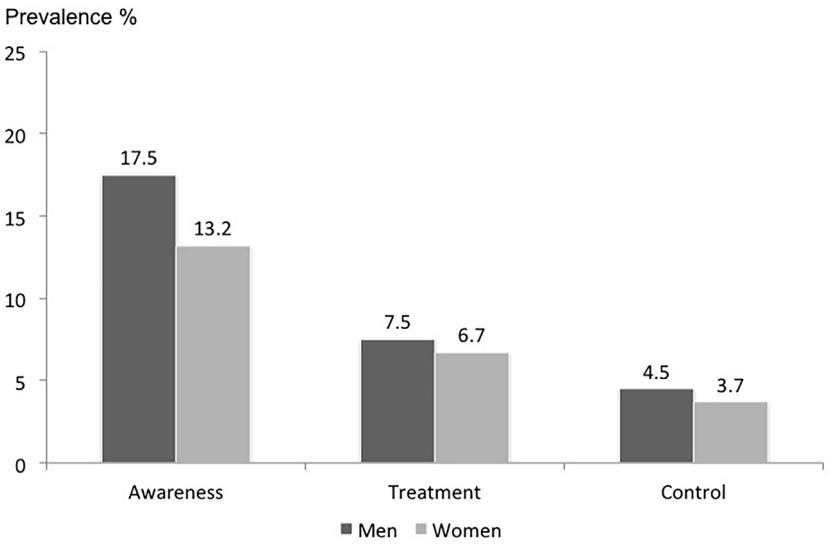

Fig. 12. Hypercholesterolemia awareness, treatment and control among urban adults in India.

serum cholesterol.[53] Borderline hypercholesterolemia (170–199 mg/dl) was in 33% and definite hypercholesterolemia was in 6.8%. Madhavan et al. evaluated lipid levels in 1201 adolescents 14–18 years in Delhi and reported centile values for various lipids.[54] Prevalence of various dyslipidemias was not reported. In another study in Delhi, Gupta et al. evaluated 1236 adolescents and young adults for dietary, anthropometric and biochemical risk factors [55]. Dyslipidemia was defined using >95% percentile values using the same cohort. In male and female adolescents, respectively, high total cholesterol was in 14% and 15%, high LDL cholesterol was in 12% and 13%, high triglycerides in 14% and 16% and low HDL cholesterol was in 5%.

A study in South India reported that prevalence of either high waist circumference, hyperinsulinemia or dyslipidemia was present in 67.7% of 12–19 years old children (n = 2640), more in overweight vs normal weight children (85% vs 65%).[56] Prevalence of high triglycerides in this study was in 24% and low HDL cholesterol was in 57%. In Kashmir valley, a study of 5–19 year old children reported that the commonest lipid abnormality in these children was hypertriglyceridemia and low HDL cholesterol, prevalence being 82% in males, 48% in females, and 37% in males and 19% in females, respectively.[57] These data show that hypertriglyceridemia and low HDL cholesterol, both markers of atherogenic dyslipidemia, are highly prevalent in Indian children.

Pune Children's Study evaluated serum lipid levels in 477 children at age 8 years and reported high cholesterol in 5.6% and high triglycerides in 7.6%.[58] These children were tracked to age of 21 years and reported significant tracking of raised cholesterol levels at age 21 years (kappa = 0.36). Positive tracking was also observed for body mass index and systolic blood pressure. More studies to track lipid abnormalities in children in India are required as evidence suggests that type of dyslipidemia in children and adults is similar.

7. Awareness, treatment and control

Epidemiological studies of hypercholesterolemia and dyslipidemia are important for developing strategies for prevention of CHD. Unfortunately there are limited data on population level prevention for high cholesterol in India using lifestyle and drug therapies. The PURE study reported a very low use of secondary prevention drugs[59] and healthy lifestyle practices[60] in low income countries including India.

We evaluated awareness of hypercholesterolemia (total cholesterol >200 mg/dl), its treatment with statins and control (total cholesterol <200 mg/dl in patients on statins) in the Indian Heart Watch study (Fig. 12).[21] Awareness was in 17.5% men and 13.2% women with high cholesterol, treatment with statins was in 7.5% men and 6.7% women, while control to targets of total cholesterol <200 mg/dl was in 4.5% men and 3.7% women. There are no similar data available from the country. In clinical practices a low use of statins among patients with CHD[61] as well as in diabetics[62] has been reported. A study has also reported that despite widespread availability the use of statins is low in India compared to many developed countries.[63]

8. Epilogue

In conclusion, this reviews shows that there are only limited studies on epidemiology of hypercholesterolemia and other dyslipidemias in India. Reports published in latter half of the last century revealed increasing trends in high total cholesterol levels. Recent multi-centric studies have reported that hypercholesterolemia, defined as total cholesterol ≥200 mg/dl, is present in 25–30% of urban and 15–20% rural subjects (Table 1). These are much lower than in high-income countries.[5] Studies have also reported that most common dyslipidemias in India are borderline high LDL cholesterol (>100 mg/dl), low HDL cholesterol and high triglycerides (atherogenic dyslipidemia). There are no national studies that have reported trends in various cholesterol lipids in India. Jaipur Heart Watch studies reported 20-year trends in various lipid levels and showed increase in mean total cholesterol, LDL cholesterol and triglyceride levels.[44] There are no large prospective studies in India that have determined association of various cholesterol fractions with CHD outcomes. Case-control studies have reported that there is significant association of acute coronary events with raised apolipoprotein B, total cholesterol, LDL cholesterol and non-HDL cholesterol and inverse association with high apolipoprotein A and HDL cholesterol.[43] Prevalence of severe hypercholesterolemia has not been well studied. There is very low awareness, treatment and control of hypercholesterolemia in India. Population-based strategies to control dyslipidemia include focus on social determinants

of cardiovascular health for prevention and efficient healthcare systems to screen, treat and control various types of dyslipidemias, specifically hypercholesterolemia and hypertriglyceridemia.[25,37,64] Clinic based management of dyslipidemias in India can be improved with better physician education, improved access to medicines as well as patient empowerment for better cholesterol self-management.[37] Focus on dyslipidemia management is urgently required in India to halt the rising tide of coronary heart disease.

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