INDIANS AND HEART DISEASE: TOP 10 THINGS TO KNOW

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It is fitting that this summary finds a place in the current AAPI Journal as it was in this journal, 3 decades ago, our first alert on this subject appeared (1990;2:5-8). The following list is distilled from our publications and especially from our review (2019; 71:99-112) and editorial (2020; 72: 65-69) in the Indian Heart Journal.

- **Coronary Artery Disease (CAD) epidemic in Indians:** According to the Institute of Health Metrics, both India and the US had ~ 600,000 CAD deaths in 1990. However by 2019, annual CAD deaths in India increased by 150% to reach 1.52 million while it decreased by 8% in the US. Rates of obesity and diabetes similarly doubled in both countries in that time period.
- **Prevalence of major risk factors (smoking, high cholesterol, hypertension, diabetes) are insufficient to explain the heightened CAD risk** (double that of whites) in South Asians. Notably, both groups have similar predicted risk by Pooled Cohort Equation and QRISK3 equation.
- **Indians are at risk of dying from a heart attack at an earlier age** (~10 years earlier than their western counterparts). Compared to white men of similar age in the United Kingdom, deaths from heart disease in Indians are 3 times higher in those younger than 30 years.
- **"Malignant CAD"** (coined by Enas and Mehta), refers to a severe and extensive atherosclerotic process involving multiple coronary arteries, with 3 cardinal features: premature onset, extreme severity, and high mortality. India, has 18% of the world's population but accounts for 30% of CAD deaths under 50 years of age.
- **Elevated lipoprotein (a) [Lp (a)], a genetic risk factor for CAD,** is likely the single best explanation for the heightened risk of malignant CAD in young Indians. Lp(a) >30 to 50 mg/dl is found in 25% of Indians, compared to 7-8% for diabetes; both conditions are associated with a two-to-three-fold risk of heart attack. Lp(a) level is genetically determined and is not affected by diet, exercise or by presently available medications.
- **Elevated Lp(a) and South Asian ethnicity are risk-enhancers** (as previously proposed by CADI Research) have now been included in the new category of Atherosclerotic Cardiovascular Disease (ASCVD) risk-enhancing factors in the 2018 American Cholesterol Guidelines to be considered for statin therapy.

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- **Deficiencies in CAD prevention at all levels:** Primordial prevention refers to a life-long healthy lifestyle (healthy diet, regular physical activity, avoidance of nicotine and obesity) to prevent the development of risk factors, whereas primary prevention refers to the control of risk factors with medication to prevent a first heart attack. Despite the availability of safe and effective medications, treatment of hypertension, diabetes and high cholesterol are dismally low in India. Only 11% of the rural population and 20% of the urban population in India have their blood pressure under control; control of diabetes is slightly better at 40% in urban India. The control of cholesterol (<200 mg/dl) is <5% even after a heart attack (secondary prevention). The importance of primordial and primary prevention cannot be overemphasized as they are mainly responsible for the dramatic decrease (50 to 80%) in CAD mortality in the US, Finland, and many other countries over the past 4 decades.
- **Reducing low-density lipoprotein (LDL) is the most beneficial and proven intervention to reduce ASCVD events.** LDL is central to the development of CAD and is both a necessary and a sufficient factor in its pathogenesis. Necessary, as atherosclerosis does not develop in the absence of some elevation in LDL and sufficient, as atherosclerosis and heart attacks develop when LDL is markedly elevated.
- **Statin drug reduces LDL and is the first-line medication for primary and secondary prevention of heart attack.** Numerous studies have demonstrated a 25% reduction in major ASCVD events per 40 mg/dl lowering of LDL. A large meta-analysis of over fifty thousand patients treated with statin have shown that "lower is better" at least down to 25-40 mg/dl. Consequently, the American guidelines abandoned the LDL goal and now uses a threshold of 70 mg/dl for initiating statin therapy analogous to the A1C threshold of 7% for blood sugar lowering. Statins are safe to use as there are no serious adverse effects (cancer, dementia, memory loss, intracranial hemorrhage, sexual and reproductive function) even at ultra-low levels of LDL (<10 to 20 mg/dl).
- **There is a need to expand the use of statins in Indians** because of 1) the increased ASCVD risk based on ethnicity (1.5- 2 fold vs whites) for any given combination of risk factors and 2) premature deaths (30% of global CAD deaths under 50 years of age are in India). The concept that statin therapy is indicated in only to those with high cholesterol is mistaken and should include all Indians with ASCVD as well as those with established risk factors and risk-enhancing factors. Accordingly, we have proposed a new simplified classification system and treatment plan: For high-risk states (diabetes, hypertension, tobacco smoking) no lipid test is needed. In others for initiation of statin therapy total cholesterol measurement is sufficient as the high cost of lipid panel testing in India is a major barrier. The intensity of statin therapy is to be matched to the degree of risk and in most Indians it would be of moderate-intensity (rosuvastatin 10 mg/day or atorvastatin 20 mg per day). If cholesterol levels remains elevated (>140 mg/dl or LDL >70 mg/dl) despite moderate-intensity statin therapy, high-intensity statin therapy may be needed (rosuvastatin 20-40 mg/day or atorvastatin 40-80 mg/day).