

Asian-Indians: a review of coronary artery disease in this understudied cohort in the United States

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Abstract: Coronary artery disease (CAD) is a major cause of cardiovascular death worldwide. Prevalence of CAD is highly variable among different races. Asian Indians have been noted to have the highest CAD rates and the conventional risk factors fail to explain this difference completely. Asian Indians constitute a fifth of the global population, and the higher rates of CAD in this population constitute a major health challenge. There have been studies in the early 2000s that investigate the risk factors in this population; however, very few studies have been done since then that explore the higher CAD rates in Asian Indians. This is a comprehensive and current review of the known risk factors for CAD in Asian Indians and strategies physicians should consider relieving this burden.

Keywords: Coronary heart disease; Asian Indian Americans; coronary artery disease (CAD)

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Introduction

Coronary artery disease (CAD) is major risk factor of myocardial ischemia, the leading cause of death in developed western countries including the United States (1). CAD is the most expensive condition treated in hospitals (2). Average CAD risks in the US population is predicted to be 2.5% (3). However, a majority of this data is collected from white adult males and is extrapolated to females, as well as other ethnic populations such as Asians and African-Americans (4). The few studies that looked at CAD risks in Asian Indians (people from India, Sri Lanka, Bangladesh, Pakistan) found an alarming rate of 3 times higher than the national average (3). Several studies that examined the CAD risk factors in this population showed an interplay between the metabolic, genetic, environmental

and social settings. However, there have been concerns over the external validity of this data since most of these studies looked at migrant Asian Indian population (5). Since this population enters an availability bias, extrapolation of this data to native Asian Indians could be erroneous (6). Despite this bias, since the CAD risk in immigrant Asian Indian population is high, strategies should be implemented that reduce this risk and prolong survival.

Epidemiology

The prevalence of CAD in the US is 2.5% (3). The prevalence of CAD risks in Indians living in India is 11% for non-diabetic patients and 21.4% for diabetic patients (7). The CAD rates from several countries and their immigrants have shown that CAD rates of the first-

generation immigrants are normally intermediate between the higher CAD rates in the country of origin and lower rates in the US (8). However, Asian Indians stand out in that their CAD rates remain higher even after immigration to US, compared to other ethnic populations (8). This suggests some non-modifiable risk factors for CAD in the Asian Indian population. CAD rates are 3 times higher in Asian Indians living in US than the US national average (3). Asian Indian immigrants have also been noted to have a higher prevalence of CAD in England and Wales, Canada, Singapore, Mauritius, South Africa, Trinidad, Fiji, Mauritius, and Qatar (8,9).

In the UK, Asian Indians have 2–3 times higher CAD prevalence compared to their national average (10). In Trinidad, CAD risks in Asian Indians are 2.6-fold higher than the white population and 7-fold higher than the black population (11). In Singapore, the incidence of myocardial ischemia, a major complication of CAD, was noted to be 3 times higher than the native Chinese population (12). Within the US (California), hospitalization of Asian Indians for CAD is 4 times higher compared to White, Japanese and Filipinos and 6 times higher compared to Chinese (8). In general, Asian Indians get hospitalized for CAD complications 2–4 times higher than other ethnic groups and 5–10 times higher for population under 40 years of age (13). A study showed that ischemic heart disease, a manifestation of CAD, has a relative risk of 1.0 for Chinese population, 1.8 for Japanese population and 6.6 for South Asian population (all living in US) compared to the US national average (14). Thus, not only is CAD more common in Asian Indians, it is also more malignant.

Within the Indian subcontinent, CAD rates in rural and urban populations differ. CAD prevalence in rural population is half that in urban population (15). CAD prevalence in rural population aged 35–64 is 6% (16). Further, CAD prevalence in urban population in India is similar to the CAD prevalence in overseas Asian Indians (8). This suggests that there may be modifiable factors that affect CAD pathogenesis in Asian Indian population.

Pathophysiology of CAD

CAD is an inflammatory condition of the blood vessels of the heart. Various metabolic factors damage the innermost lining of blood vessels, which trigger an inflammatory reaction. Cytokines, metalloproteinase and other

inflammatory molecules attract immune cells and this forms an atherosclerotic lesion (17). As connective tissue and lipids fill the core of this lesion, a fibroma develops that is capped by endothelial lining and smooth muscle cells. Macrophages within the fibroma engulf lipids and oxidize them to form foam cells (18). Oxidized lipids within foam cells play a vital role in the stability of the fibroma (19). A destabilized fibroma can rupture leading to a thrombus formation and subsequent embolization of said thrombus. Alternatively, the fibroma grows in size until it significantly occludes the artery, subsequently causing ischemia of the tissue.

Cholesterol plays a vital role in atherosclerotic plaque formation. Statins are a class of drugs that inhibit an enzyme in cholesterol synthesis pathway called HMGCoA reductase (20). Thus, statins reduce serum cholesterol and have proved efficacious in management of CAD (21).

Risk factors

Conventional risk factors for CAD have been extensively studied. Obesity (22), diabetes (23), hypertension (24), dyslipidemia (25), metabolic syndrome (26) and smoking (27) are all highly associated with CAD development. However, these risk factors do not account for the increased prevalence of CAD and mortality associated with CAD seen in Asian Indians. More than 50% of CAD associated death in India occurs before the patient reaches the age of 50 years (28) and 25% of myocardial infarction (MI) occur before the age of 40 years (29). Heart disease is occurring in Asian Indians 5–10 years before other ethnicities (30) because the CAD shows accelerated atherogenesis which results in higher premature morbidity and mortality (31). Since Asian Indians have a lower prevalence of conventional risk factors such as hypertension, hypercholesterolemia, obesity and smoking (8,13,32) it is important to explore the underlying causes of increased CAD prevalence.

Modifiable factors

Considering the disparity in CAD prevalence in Asian Indians in rural and urban settings, it can be inferred that there are risk factors such as nutrition and environment that play a role. Urban Indians have a body mass index (BMI) of 24–25, compared to rural Indians whose BMI is about 20 (8). While BMI is not extremely high, abdominal obesity is more common in urban setting with men having waist-to-hip ratio (WHR) of 0.99 compared to 0.95 for

rural men (8). This increased abdominal obesity is a risk factor for dyslipidemia, diabetes, and insulin resistance (8). Further, Asian Indians in general are less likely to exercise compared to white population (33). This sedentary lifestyle promotes obesity. High intensity aerobic exercise (34) and moderate alcohol intake have been known to reduce risk of CAD and MI (35). Studies have shown low consumption of alcohol in the Asian Indian population (36).

Type 2 diabetes prevalence in Asian Indians in US has been reported to be at 18.3% for ages above 20 years. This is higher than the average of Indians living in India which is between 12.1–14.0% (37). It is almost 3 times higher than the US average of 5.3% and 4 times higher than the white population average of 4.8% for similar age groups (38). About 50% of Asian Indians are vegetarians and yet their CAD and diabetes risks are comparable to or higher than non-vegetarians as seen here (8). This is attributed to the liberal use of high fat dairy, butter, ghee, cheese and paneer in their everyday meals. Kerala, a state in southern India, uses coconut oil in meal preparations, and citizens of this state were found to have the highest rates of CAD in India (8). Reusing oil for cooking in Asian Indian cultures is common and it increases risk of CAD development (8). A recent study showed that Asian Indians eat less fruits and vegetables in their regular diet and this has negative implications on CAD (36). Thus, unhealthy and high-caloric diet (39) together with the sedentary lifestyle increases CAD risks in Asian Indians (40).

The INTERHEART study showed that hypertension and diabetes are important risk factors for CAD development in Asian Indian women compared to men (41). While hypertension is less prevalent in the Asian Indian population (32), when present, it is more commonly associated with high morbidity and mortality compared to whites (42). Tobacco use (cigarettes and beedi) is strongly associated with CAD in Asian Indian (8); however, smoking rates are lower in Asian Indian population living in US (43). A few studies have estimated smoking prevalence at 28.5–30% in Indians living in India (44,45). A study showed 17.1% prevalence in Other Asians (Indians, Japanese, Korean and Pacific Islander) vs. 25.5% in non-Hispanic white men (46). There are many studies showing high prevalence of insulin-resistant diabetes, central obesity and dyslipidemias with low high density lipoprotein (HDL), elevated triglyceride, low dose lipoprotein (LDL) and lipoprotein a (8,32,33). However, diabetes and metabolic syndrome cannot fully explain the high CAD rates in this population (47).

Non-modifiable factors

Since CAD risk in the Asian Indian population do not decline upon immigration to foreign countries with lower CAD risks, a genetic link is likely. Furthermore, clustering of CAD in Asian Indian families indicates genetic risk factor/susceptibility (48). Coronary Artery Disease Genome-wide Replication and Meta-analysis (CARDIOGRAM) study and other genome-wide association studies (GWAS) have found 109 loci associated with CAD and can explain 28% of the heritability (49,50). One likely explanation for the low heritability can be the polygenic nature of CAD. Another GWAS found 45 loci in European and South-Asian population that are associated with CAD (1). Therefore, there are multiple genes which regulate risk factors for CAD.

Studies on Asian Indians have found elevated levels of Lipoprotein(a) [Lp(a)]. Lp(a), which is a strong risk factor for CAD (8). Homocysteine has also been associated with increased risk for CAD and Asian Indians have higher levels of homocysteine (51). A study noted that C-reactive protein (CRP) levels in South Asian women were double compared to European women and these CRP levels were associated with central obesity (52). Since CAD is predominantly an inflammatory disease, elevated CRP levels can indicate elevated risks in this population.

Social factors

Asian-Indians have the largest foreign-born population in the US. The recent surge in immigration has been from the educated middle class. As this population acculturates to the US customs, their diets change from high intakes of saturated fats and refined carbohydrates to healthier options. They also partake in leisurely physical activities (53). These healthier life-choices along with higher education support the “healthy immigrant effect” which describes that immigrants are normally the healthier fraction of the population they left behind (54). However, Asian-Indians living in California have reported the highest mortality rates from CAD complications compared to other ethnic subgroups (55). Studies have shown that Asian-Indians in US often eat high carbohydrate diets and have uneven meal patterns. They are working longer hours and have considerable stress. A study showed that acceptance in the new society was a major factor contributing towards psychological well-being. Factors such as number of years in US, US education, gender and family income

played a minor role in development of stress (56). Thus, immigrants who had more cultural and social ties in US and fewer traditional ties reported better mental health status. Further, the sedentary lifestyle increases obesity risk. This is associated with high LDL cholesterol and higher in-turn prevalence of CAD (57).

Socio-economic status also plays a role in CAD. Poor living conditions in early life and lack of education have been associated with higher prevalence of CAD in the Asian Indian population (58). Poor people in rich countries and rich people in poor countries suffer from CAD (59). Further, there may be some psychological factors associated with immigration that play a role in adverse health-related decisions. Since Asian-Americans are the fastest growing ethnic group in US, it calls for more studies examining CAD risks in these population (60).

Further, they often have lower rates of health insurance. Except for Vietnamese populations, all other Asian subgroups have un-insurance rates of 12.8–14.5% (61). The immigrants often lack proficient English which can become a barrier towards acquiring healthcare benefits (62). Healthcare literacy has also been identified as a factor leading to lower rates of health insurance in this population (63). The Hindu religion can also impede access to healthcare. Hinduism is based off the concept of “Karma” which describes that current circumstances arise due to actions in past lives (64). Therefore, many ailments are seen as justice from god rather than physiological aberrations and thus healthcare is not utilized.

Strategies to reduce CAD

Promoting education and awareness about the pathogenesis of CAD and the higher rates in this population can improve routine health maintenance. Discouraging cigarette smoking and adapting an exercise routine can promote better cardiovascular health. Asian Indians should also consider their eating choices. Reducing high fat dairy and increasing daily intake of fruit and vegetables can improve health. Physicians can lower threshold for prescription of anti-atherosclerotic medications like statins. The optimum triglyceride levels in Asian Indians appears to be 150 mg/dL compared to the 200 mg/dL for others in western society (65). Therefore, aggressive screening tests for CAD in Asian Indians is beneficial.

Conclusions

Relative risk of CAD associated mortality in Asian Indians is 20–50% higher than other populations (66). Since Asian-Americans are the fastest growing ethnic group in the US, more studies examining CAD risks in these population are indicated (60). Further, studies that look at CAD risks in Asian populations, grouping them as one may potentially mask the heterogeneity within this group (53). There need to be more studies focusing just on Asian-Indian populations, the risk factors associated with CAD and strategies to reduce CAD.

With a growing Asian Indian population in the US, physicians will be seeing more Asian Indian patients. Consequently, it is important for physicians to know about their increased CAD risks so that appropriate treatments can be started earlier in the course.

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Footnote

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