# Risk Factors for Atherosclerotic Cardiovascular Disease in the South Asian Population

Clinical Advisor

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**Highlight:** South Asians exhibit the highest rates of ASCVD among all ethnic groups, and the highest prevalence is in younger age groups; up to 25% of myocardial infarctions in India occur in individuals younger than 40 years of age.

# **Body**

Advanced practice clinicians need to be aware of the high rates of <u>atherosclerotic cardiovascular disease</u> (ASCVD) in the South Asian population. The most common cause of noncommunicable disease death worldwide is due to ASCVD,1 and ASCVD is a key driver of health disparities globally; 80% of the ASCVD burden occurs in low- and middle-income countries.2

South Asia is the fastest growing region in the world.3 The South Asian population - defined as those living in India, Nepal, Maldives, Bhutan, Afghanistan, Pakistan, Sri Lanka, and Bangladesh4 - constitute 20% of the world's population; people from these countries are at particular risk for ASCVD.1 Within the next 15 years, India is projected to become the most populous nation on Earth. South Asians have a greater prevalence of ASCVD than other ethnic groups and have disproportionately poorer health outcomes overall compared with other ethnic groups3; 50% of the population is more likely to die from coronary heart disease compared with those of European origin.5

#### [HMICMS AD]

It is important to note there are established differences in morbidity and mortality among different ethnic groups within the South Asian population.6 However, ASCVD death occurs 5 to 10 years earlier in all South Asian populations compared with Western populations.7 Although ASCVD rates in the United States and other developed countries have decreased by half in the past 30 years, the rates in South Asians have doubled in the past 20 years.1,7 The explanation for this increase in ASCVD may arise from complex interactions between genetic and environmental factors.3 South Asians exhibit the highest rates of ASCVD among all ethnic groups, and the highest prevalence in this disparity is seen in younger age groups.8 Up to 25% of myocardial infarctions in India occur in individuals under the age of 40 compared with 4% to 6% of individuals in Western Europe and North America.8 It is

projected that within the next 10 years, South Asians will account for >20% of ASCVD deaths worldwide.9 This results in the highest loss of potentially productive years of life due to ASCVD.

Many risk factors are strongly linked to the development of ASCVD, including elevated blood glucose, obesity, smoking, elevated blood pressure, abnormal cholesterol levels, and a positive family history of ASCVD. However, these factors do not fully explain the disproportionately high ASCVD risk within the South Asian population. This residual risk suggests that additional, nonclassic risk factors contribute to ASCVD risk.

#### [HMICMS RELATED ARTICLES]

Attempting to reduce the excess morbidity and mortality of ASCVD requires a wide understanding of the collective risk factors associated with the disease state to facilitate treatment and attempt a reduction of risk across a population. However, population-specific risk factors among the South Asian population have been inadequately explored, leading to a significant gap in the ability to understand ASCVD risk factors within this population. The increasing global ASCVD burden in developing countries and the increasing cost of health care on local economies are cause for concern.

In addition to the risk of heart disease, other health issues exist specifically in South Asian populations. They are 3-to 4-times more likely to have <u>type 2 diabetes</u> than whites, have a faster progression of disease, be diagnosed at a younger age, and have more complications.10

#### Genetic Risk Factors

#### Cholesterol

Dyslipidemia is well documented as one of the main risk factors of ASCVD. The effects of hypertriglyceridemia, hyperglycemia, and increased free fatty acid levels, both fasting and postprandial, on endothelial dysfunction may be mediated through oxidative stress.11 Although dyslipidemia does not occur at a higher rate in South Asians, the type of dyslipidemia does differ. When compared with Chinese and European populations, South Asians have higher total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels, and lower high-density lipoprotein (HDL) cholesterol levels.12 South Asians also have genetic polymorphisms causing higher levels of elevated lipoprotein (a) and defective apolipoprotein B.13 Both of these polymorphisms are independently and highly correlated with the presence and severity of ASCVD.

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#### Hypertension

South Asians have upregulated angiotensin-converting enzyme (ACE) activity that is directly correlated with the development of hypertension.14,15 Das et al16 describe polymorphism of the *ACE* gene in adult Asians as a probable genetic risk factor for developing hypertension. A replication study and meta-analysis of >21,000 Japanese adults with hypertension confirmed the relationship of the genetic link and hypertension in the Asian population.17 Based on the genetic predisposition for development of hypertension, ACE inhibitors should be considered in therapeutic treatment regimens for the South Asian population.

#### Hyperglycemia

Individuals with diabetes die on average 10 years before individuals without diabetes, and two-thirds of those deaths are attributed to ASCVD.9 According to the International Diabetes Federation, more than 21 million Asian Indians have prediabetes.18 South Asians have a higher incidence of diabetes compared with non-Hispanic whites. However, even without overt diabetes, South Asians have reduced insulin sensitivity, up to 4-fold higher18 compared with other racial and ethnic groups, which can be explained by increased visceral fat and genetic polymorphisms.13 Older age, female sex, physical activity, and adiposity are strong indicators of insulin sensitivity, and each of these may alter the relationship of hyperglycemia to oxidative stress and ASCVD risk. The prevalence of type 2 diabetes is more than 4 times higher in South Asians than in other ethnic groups, and the onset is as much as 10 years earlier.4 South Asians have more insulin resistance in fasting and postprandial states than other

ethnic groups,19 and one-third of South Asians have metabolic syndrome,9 possibly a consequence of increased obesity and ectopic fat deposition.

# Adiposity

Among nations categorized as "major" by the Organisation for Economic Co-operation and Development, India has the lowest rate of obesity in the world.9 However, South Asians are much more susceptible to the deleterious metabolic effects of visceral adiposity. Visceral adiposity is well established as a direct risk factor associated with ASCVD globally but is more prevalent in the South Asian population in any body size.20 Visceral adipocytes, not subcutaneous adipocytes, are directly linked to increased inflammatory cytokines and the development of a proinflammatory state.21 South Asians exhibit the unique and deleterious obesity phenotype of increased visceral adipose tissue and lower lean body mass independent of waist circumference or body mass index.20

Although the most accurate measurement of visceral adiposity is computed tomography, this option is not feasible, equitable, or efficient. Visceral adiposity is often measured with a waist-to-hip ratio. Healthy waist circumferences for most adult populations are <88 cm for women and <102 cm for men. However, recent guidelines specify that people of South Asian ethnicity should have waist circumferences <85 cm for women and <90 cm for men.9

The greater prevalence of visceral adiposity when compared with generalized obesity suggests rapid fat gain in a previously lean individual.5 This type of fat gain places these individuals at higher risk for diabetes and metabolic syndrome and is thought to contribute significantly to ASCVD risk.8

#### **Tumor Necrosis Factor**

With increased insulin resistance, there is a subsequent increase in circulating proinflammatory cytokines such as tumor necrosis factor-alpha, interleukin 6, and interleukin 18.11 South Asians have significantly increased high-sensitivity C-reactive protein (hs-CRP), which indicates a chronic low-grade state of inflammation.4

#### Nonalcoholic Fatty Liver Disease

South Asians have a genetic predisposition to development of nonalcoholic fatty liver disease (NAFLD), or hepatic steatosis, which is a significant risk factor for ASCVD. NAFLD is exacerbated by a high-sugar diet and abdominal adiposity, which are also prevalent in the South Asian culture.9 Because NAFLD is often asymptomatic, the majority of individuals are unaware of their condition. The prevalence of NAFLD (approximately 30%) is similar between South Asian and Western populations; individuals are predisposed to not only ASCVD and cirrhosis but to hepatic and other extrahepatic malignancies.9 The increased ASCVD risk associated with NAFLD is independent of standard ASCVD risk factors.

Regression and resolution of NAFLD is primarily accomplished through exercise, abstention from alcohol, weight loss through intra-abdominal fat mobilization, and a diet low in sugar and refined carbohydrates. These behavioral modifications are often the first-line treatment for other comorbid conditions that commonly affect South Asians.

#### Vitamin D Deficiency

Previous evidence indicates that vitamin D deficiency and insufficiency are becoming global epidemics.22 It is estimated that 1 billion people worldwide have vitamin D deficiency.23 Multiple epidemiologic studies continue to highlight vitamin D deficiency as a marker of cardiovascular risk, promoting accelerated atherosclerosis and subsequent cardiovascular events.24-26 There are rising concerns regarding the level of vitamin D in South Asian populations. Nimitphong et al27 reported the existence of a high prevalence of vitamin D deficiency in South Asians. The vitamin D deficiency is predicted to be as high as 70% in this population, in comparison with citizens of Western countries, where studies indicate that vitamin D deficiency is present in only 20% to 25% of the total population.22,28-30 Poverty and lack of healthcare literacy regarding vitamin D deficiency remain underlying determinants that provoke vitamin D deficiency in South Asians.27,31 Failure to associate the deficiency with inadequate exposure to sunlight, skin pigmentation, and insufficient consumption of dietary vitamin D compound the

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issue. In addition, cultural practices may discourage skin exposure and variation of the traditional South Asian diet, which is typically low in vitamin D-containing foods.32

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#### **Environmental Factors**

Due to rapid cultural modernization and transformation from a rural agrarian population to an urban sedentary population, and the propensity of genetic factors to take several years to display their effects, a greater emphasis has been placed on modifiable environmental ASCVD risk factors.11

#### Migration

The general health status of migrants, both within South Asian countries and internationally, is well studied. Well-settled migrants in high-income countries achieved rapid socioeconomic prosperity; however, rural-to-urban areas in low-income countries remained poor and became unhealthier.5 Rural-to-urban migration in South Asia is associated with decreased physical activity, higher intake of dietary fats, lower intake of fruits and vegetables, truncal obesity, hypertension, and other cardiometabolic abnormalities associated with increased cardiovascular risk.5 The general health status of migrant women has been demonstrated to be inferior to that of migrant men.5

Geographic location of South Asian people may be the strongest cardiovascular risk factor discovered and is multifactorial; it includes inadequate health care and infrastructure, high levels of poverty, and remote locations.33 Over the past 50 years, as South Asian countries have become rapidly industrialized, the prevalence of hypertension, obesity, hypercholesterolemia, and type 2 diabetes has increased significantly.

# Physical Activity

Regular physical activity plays a significant role in lowering the risk of heart disease. Unfortunately, the prevalence of sedentary lifestyle remains high in South Asians.20 South Asian women are less likely to participate in physical activity than other populations.20 More than 90% of adults of South Asian ethnicity report no recreational exercise during leisure time.9 Increased aerobic physical activity has been demonstrated to reduce visceral adiposity and ASCVD risk independent of weight loss in white populations; however, until recently, this has not been studied in South Asian populations.20 Lesser et al20 found that South Asians did not have a consistent reduction in visceral adiposity with moderate-intensity exercise but did demonstrate a regular reduction with vigorous-intensity exercise. This may suggest an ethnic-specific response requiring a greater exercise stimulus to mobilize fat cells.

Active travel to and from work has been promoted within the South Asian population to decrease ASCVD risk. Gordon-Larsen et al34 found that active commuting was inversely related to obesity, elevated body mass index, blood pressure, and triglyceride and fasting insulin levels, and positively associated with elevated HDL cholesterol levels. Individuals who actively travel to and from work have higher overall physical activity levels and are less likely to be overweight or obese.35 Current World Health Organization guidelines recommend >=150 minutes of moderate-intensity or 75 minutes of vigorous-intensity exercise per week; more than 50% of the population does not meet these recommendations.9 It is of paramount importance to encourage the inclusion of exercise in the daily routine and to build infrastructure to support these recommendations.

#### Diet

Important ethnic customs and cultural beliefs influence dietary intake, and the South Asian population is often exposed to high-fat, high-carbohydrate, and low-protein and low-fiber diets beginning in childhood. These negative dietary patterns are correlated with increased inflammatory markers and insulin resistance in the South Asian population.11 Specifically, an increase in white rice consumption, a staple of the South Asian diet, has been correlated with an increased risk of type 2 diabetes; the same correlation was made with increased consumption of refined grains.11 High-fat and high-carbohydrate diets also increase plasma endotoxin levels, which, by downstream effect, increases insulin resistance and inflammatory markers. South Asians consume large amounts

of hydrogenated fat, ghee, butter, milk, ground nut oil, trans-fatty acids, and coconut oil, compounding these dietary risks.

Refined sugar was invented in India in approximately ad 350, and India is the largest consumer of refined sugar in the world. In South Asians, particularly Indians, consumption of a large amount of sweetened food and beverages is popular.36 The consumption of sugar-sweetened foods is important to many traditions within the Indian culture, and it is customary to "sweeten the mouth" after each meal.9 Although sugar is a significant source of calories and a fundamental aspect of the Indian culture, the consumption of refined sugar and carbohydrates poses a significant threat to the long-term health of an increasingly sedentary population with an innate predisposition to type 2 diabetes and metabolic syndrome. Recent socioeconomic changes and cultural beliefs within the South Asian population have contributed to the amplification of these negative dietary habits and predisposed an entire population to increased prevalence of ASCVD.

Dietary fiber and protein intake was negatively associated with insulin resistance, inflammatory markers, and improvement in ASVCD risk in South Asians; similarly, dietary intake of fruits and vegetables was negatively associated with insulin resistance and inflammatory markers in the same population. A low-protein diet was positively associated with islet cell dysfunction in South Asians.11

Regardless of how much the South Asian diet contributes to ASCVD, the diet is of central importance to cultural identity.8 Dietary suggestions often challenge the core principles of the South Asian diet, and it is thought that adhering to these suggestions makes someone less South Asian and more American.

#### **Smoking**

There is a high prevalence of cigarette smoking and smoke exposure in the South Asian population. This identifies the great need to implement smoking prevention and cessation efforts. Tobacco-related deaths are highest in India, where 80% of the world's tobacco users reside. One million deaths annually are linked to some form of tobacco use. Approximately one-third of the population in India aged >=15 years uses tobacco products. In India, 5500 youths initiate tobacco use every day. Current tobacco use has been documented in 14.6% of school-going youths aged 13 to 15 years.37

Tobacco use in people living in low socioeconomic areas is high. In India, approximately 75% of children live in slums and low-resource settings. In these communities, evidence suggests that tobacco use starts in children as young as 6 years of age. Children in these environments lack the knowledge and skills to resist tobacco use and give in to social influences, including peer pressure, to use tobacco in a tobacco-friendly environment.37

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Tobacco use is a modifiable risk factor that is relevant to the global burden of chronic diseases. The duration of tobacco use is an additional factor that needs to be considered. Some people go through start-quit-restart cycles; therefore, total exposure to tobacco use must be taken into consideration as a risk factor for chronic diseases.38

Smokeless tobacco and bidis are commonly used in India and Bangladesh; however, manufactured cigarettes are preferred by most tobacco users.39

The highest prevalence of smoking in India is in adolescent boys and men aged 15 to 29 years. Education levels and literacy are related to tobacco use; individuals with higher levels of education use less tobacco than individuals with lower education levels. The absolute number of adolescent boys and men aged 15 to 69 years has increased significantly in India over the past 15 years.40

#### Stress

A large body of literature demonstrates that, in ethnic minorities, chronic <u>stress</u> and disease exposure are linked to increased ASCVD.41,42 The belief that acquiring diseases such as diabetes or ASCVD is not under an individual's control is prevalent among South Asians.8 This can be explained by the large spiritual foundation within the South Asian culture and the belief that much of life is in a higher power's control and cannot be modified by the individual.

#### Conclusions

The South Asian population has many genetic risk factors for ASCVD and needs to be monitored, screened, and treated appropriately to prevent ASCVD. Education also needs to be provided to encourage healthy diets and physical activity. This population is at higher risk for cardiovascular incidents at much younger ages. It is essential that providers be aware of the increased cardiovascular risk factors among this population. Providers need to be diligent to appropriately treat this population to prevent cardiovascular incidents. The advanced practice clinician is particularly well positioned to proactively screen and treat the South Asian population for ASCVD.

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