Angiology
2015, Vol. 66(5) 405-415
© The Author(s) 2014
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/0003319714541323
ang.sagepub.com
SAGE

South Asian Ethnicity and Cardiovascular Risk: The Known, the Unknown, and the Paradox

Emad Ahmed, MBChB, MD[1,2] and Ayman El-Menyar, MBChB, MSc, FRCP, FESC, FACC[3,4,5]

Abstract

South Asians (SAs), in their countries or after migration, are at high risk of coronary artery disease (CAD) and mortality compared to other ethnic groups. It has been shown that >90% of CAD global risk could be attributed to 9 modifiable risk factors (RFs) worldwide. However, these conventional RFs may not fully explain this high risk of CAD among SAs. Therefore, attention has been directed toward nonconventional RFs. In this narrative review, we evaluate the conventional and emerging cardiovascular RFs characterizing SAs. These factors may explain the high morbidity and mortality among SAs. Further prospective studies are urgently needed to set algorithms for the optimal management of these RFs in high-risk populations like SAs.

Keywords

cardiovascular risk factors, ethnicity, South Asian

Overview

"Race" and "ethnicity" are complex terms that are often used interchangeably. Race is a social category with shared external characteristics and social history which is biologically invalid.[1] Ethnicity is a cultural phenomenon with overlapping features such as descent, culture, society, food, and language.[1,2] There is increasing evidence indicating that race and ethnicity affect health through complex and dynamic interactions of associated factors. For example, biological factors such as smoking and obesity are risk factors (RFs) for heart disease and are linked with social, political, and economic factors such as income, deprivation, access, education, barriers, language differences, racism, different health systems, and social networks.[1,3-5]

South Asian (SA) ethnicity represents individuals whose ethnic roots originate from the Indian subcontinent, a large geographic area that includes India, Pakistan, Bangladesh, Sri Lanka, Nepal, Maldives, and Bhutan. There is considerable existing and ongoing research aimed at explaining the higher incidence of coronary artery disease (CAD) in SAs living in SA countries or abroad.

Burden of CAD in SAs

Currently an epidemic of CAD is in progress among SAs worldwide. Despite the fact that nearly half are lifelong vegetarians, SAs have the highest rate of CAD among all populations.[6] The Singapore Autopsy study reported 7 times higher rate of coronary atherosclerosis in SAs compared with the Chinese.[7]

Coronary angiogram studies revealed that 3-vessel disease was seen among half of all SAs and one-third of premenopausal women.[8-10] Unlike for whites, comparative studies described CAD in young SAs as severe, extensive, and malignant.[11-13] This can be attributed to an accelerated atherosclerotic process that begins early in life. Epidemiological studies among people of SA origin, irrespective of their place of living, suggest that the likelihood of developing CAD in SAs is about 2-fold higher than in Europeans and 5-fold higher than in Chinese.[14-18] South Asians are prone to developing CAD at a younger age, often before the age of 40 years in men.[19,20] A previous angiographic study in Malaysia reported that SAs younger than 40 years had a 15-fold higher rate of CAD compared with Chinese and a 10-fold higher rate compared with Malays.[21]

In India, about a quarter of acute myocardial infarction (AMI) occurs in individuals younger than 40 years and half in individuals younger than 50 years.[22] In general, myocardial infarction

[1] Cardiology Department, Heart Hospital, Hamad Medical Corporation, Doha, Qatar
[2] Cardiology Department, National Heart Institute, Cairo, Egypt
[3] Clinical Medicine, Weill Cornell Medical School, Doha, Qatar
[4] Clinical Research, Hamad General Hospital, Doha, Qatar
[5] Cardiology Unit, Internal Medicine, Ahmed Maher Teaching Hospital, Cairo, Egypt

Corresponding Author:
Ayman El-Menyar, Weill Cornell Medical College and Hamad General Hospital, PO Box 3050, Doha, Qatar.
Email: aymanco65@yahoo.com

Table 1. Risk Factors for Future Cardiovascular Event in South Asian.

Category	Risk Factors
Conventional nonmodifiable risk factors	1. Age 2. Sex 3. Race 4. Family history of premature CAD 5. Genetic • Thrifty gene • Lipoprotein(a)
Conventional modifiable risk factors	1. Hypertension 2. Dyslipidemias ↑TC,↑LDL-C, ↑TG, ↑ApoB/ApoA-1 ratio, ↑TC/HDL ratio, ↓HDL-C 3. Obesity (central/abdominal) 4. Smoking 5. Atherogenic diet • High calorie, high fat, low fruits and vegetables 6. Alcohol consumption 7. Lack of leisure-time physical activity 8. Diabetes mellitus (type 2) • Insulin resistance • IGT 9. Metabolic syndrome 10. Psychological factors Mental stress and depression 11. Socioeconomic factors 12. Low educational level
Nonconventional (emerging) risk factors	1. Dysfunctional HDL-C 2. CRP 3. Elevated thrombogenic risk factors ↑Fibrinogen, ↑PAI-1, ↑Lp(a), ↑platelet activity, ↓endogenous fibrinolytic activity 4. Elevated inflammation markers (adipokines) 5. Microalbuminuria 6. Telomere length 7. Fetal programming 8. Small mean coronary artery diameters 9. Coronary artery calcification 10. ↑Homocysteine 11. ↑sd LDL-C particles

Abbreviations: ApoB/ApoA-1 ratio, apolipoprotein B/apolipoprotein A-I ratio; CAD, coronary artery disease; CRP, C-reactive protein; ↓, decrease; ↑, increase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; IGT, Impaired glucose tolerance; Lp(a), lipoprotein(a); PAI-1, plasminogen activator inhibitor 1; TC, total cholesterol; TG, triglyceride; sdLDL-C, small dense LDL-C.

(MI) develops 5 to 10 years earlier in SAs than in other populations,[12,23] and its occurrence in patients younger than 40 years is 5- to 10-fold higher.[24] The CAD mortality rate among overseas SAs is 50% to 300% higher than that of Europeans, Americans, and other Asians irrespective of gender, religion, or social class.[25] The CAD mortality rate among SAs younger than 30 years is 3-fold higher than for whites in the United Kingdom and 10-fold higher than the Chinese in Singapore.[6,26]

Immigration, Urbanization, and Changing Diets

Lifestyle changes brought by urbanization, industrialization, and globalization may promote CAD. Increased consumption of tobacco and alcohol, consumption of energy-dense and processed foods, access to vehicles, less physical activity, and psychosocial RFs are of concern.[18,27]

Urbanization is occurring at a faster rate in India. By 2026, urban growth in India is predicted to be 67% of the total population growth and 38% of the population will be urban, compared with 28% in 2001.[28] Previous studies had reported a high prevalence of obesity as a result of decreased physical activity among urban dwellers in India. Insufficient physical activity was reported in 14.7% of the urban population compared with 12.2% in the rural population.[29] The Indian Industrial Population Study adopted the link between the ''reversal of social gradient,'' behavioral RFs (ie, tobacco use and insufficient physical activity), and the prevalence of hypertension among the lower socioeconomic class.[18]

The level of education may influence cardiovascular (CV) RFs as shown by Reddy et al.[18] These authors found that compared with the periurban group with no formal education, the education group was characterized with greater leisure time

physical activity (42% vs 13%), less tobacco use (12% vs 77%), and lower prevalence of hypertension (23% vs 31%).

The impact on the health of migrants is complex as origins of immigrants are increasingly diverse. The "healthy immigrant effect" refers to better health status of immigrants when compared with that of the native-born population.[30] This happens mostly due to a selective immigration process where only people who have passed a medical screening are granted entry to that particular country.[30,31] Nevertheless, studies have shown that their health status tends to decline with the years spent in the host country. Immigrants experience transitions in many segments of their life while relocating to a new country that may result in cultural, psychosocial, socioeconomic, lifestyle, and social support network changes.[31] With increases in time since immigration, these changes in the lifestyle of immigrants may result in an increased number of CV RFs.[32] The healthy immigrant effect decreases over time while measures of silent CV disease increase and eventually exceed that of nonimmigrants.[33] A significant positive relationship between the prevalence of coronary artery calcification score and time since immigration among Chinese and black immigrants in the United States has been reported.[34] Furthermore, time since immigration was shown to be a significant predictor of carotid intimal–media thickness (cIMT), a measure of silent heart disease, after adjusting for sociodemographics, ethnicity, lifestyle characteristics, and cardiometabolic RFs.[32] The study showed that there was a 2% increase in cIMT for every 10 years since immigration in addition to the 7% increase in cIMT for every 10 years of age.[32]

Mooteri et al concluded that the duration of residence was an independent predictor of self-reported CAD among SA immigrants in the United States.[33] Studies have shown that immigration may lead to adoption of healthy behaviors, especially in Western countries. Leisure time physical activity tends to increase and smoking rates tend to decrease among immigrants with time since immigration in Western countries.[35] Chinese immigrants reported a greater consumption of fruits and vegetables and a greater awareness and knowledge about healthy foods since their immigration to Canada.[35] The Coronary Artery Disease in Indians (CADI) study demonstrated a 10% prevalence of CAD among first-generation SA immigrants to the United States compared with a 2.5% among the general population in the Framingham study.[19] In an analysis of age-standardized CAD mortality in Canada, SAs had the highest mortality rate compared with individuals of Chinese and European descent.[36]

Migration Within the Country

In low-income countries, migration from rural to urban areas is associated with increased cardiometabolic RFs and CAD.[37,38] These changes are influenced by changes in physical activity, dietary fat intake, and duration of migration.[37]

In India, the higher rate of CAD in urban compared to rural area mainly reflects the roles of nutritional and environmental factors.[39] Previous data showed that the prevalence of CAD in the Indian urban area is about double the rate in the rural area and about 4-fold higher than in the United States.[39] According to Gupta et al, there was a significant correlation of duration of migration with certain RFs such as waist size, waist to hip ratio, and systolic blood pressure in rural–urban migrants.[37] In that study, the median urban exposure was 9 years, while in the India Migration Study, it was 26 years.[37,40]

Furthermore, the pattern of CAD in India shows a higher rate in the urban and rich, followed by the poor and rural people; this pattern is similar to that seen in the United States.[39]

South Asians in the United Kingdom have higher CV RF load compared with their siblings living in India.[41] Therefore, adverse changes in CV RFs and disease rates are observed when SAs adopt an urban lifestyle whether they live in India or abroad.[37,38,41] The higher rate of CAD in urban areas is coupled with an increase in the rate of lipid and glucose abnormalities, hypertension, and obesity among urban compared with rural populations.[42]

Why SA People are at Risk in a New Country?

Various studies in migrant SA populations have confirmed a 3- to 5-fold increase in the risk of MI and CV death compared with other ethnic groups.[43] The increased risk of SAs reflects an adverse combination of gene–environment interactions on migration.

The conventional RFs reported in many studies are attributed mostly to a higher levels of 9 modifiable RFs in SA countries.[1,14.43-47] These 9 RFs include low consumption of fruits and vegetables, smoking, alcohol consumption, psychosocial factors, sedentary lifestyle, hypertension, dyslipidemia, central obesity, and diabetes mellitus (DM).

Risk factors increase with urbanization or migration, producing a "typical pattern" of insulin resistance, pre-DM particularly impaired glucose tolerance (IGT), DM, abdominal obesity, metabolic syndrome, low high-density lipoprotein cholesterol (HDL-C), high triglyceride (TG), increased low-density lipoprotein cholesterol (LDL-C) levels, and hypertension.[1,3,8,14,39,43-51] South Asian culture encourages overconsumption of high salt, saturated fat and high-glycemic index foods, and reduced exercise with social, cultural, and other barriers to change.[43-47] Among SAs, the interaction of the emerging and thrombogenic RFs with the "typical" lipid abnormalities produces synergistic effects with conventional RFs.[43,44] Enas et al showed that immigrant Asian Indian men in the United States have high prevalence of CAD, DM, low HDL-C levels, and high TG.[19] In that study, the mean duration of immigrant stay in the United States was 18 years.

South Asians and CV RFs

We divided RFs in SAs into conventional RFs and nonconventional RFs.

Conventional RFs. As in other populations, the risks of CAD among SAs are significantly associated with all conventional CV RFs. However, compared with whites, SAs have a lower

prevalence of hypertension, hypercholesterolemia, obesity, and smoking but a higher prevalence of high TG, low HDL-C, IGT, and central obesity.[39]

The INTERHEART study showed that more than 90% of the person attributable risk of CAD can be explained by the 9 modifiable RFs.[47] The study also found that the person attributable risk for each of these RFs not only varied by age and sex but also across geographical regions.[47]

The SA component of INTERHEART study reported variations in the mean age of presentation of CAD between SA countries and deaths attributable to MI in SAs occur 5 to 10 years earlier than in Western populations.[52] South Asian men who sustained acute MI were 5.6 years younger than women. The higher risk of premature CAD is largely determined by the higher levels of RFs and the 9 conventional RFs collectively explain 86% of the acute MI risk in SAs. Moreover, in SAs, abnormal apolipoprotein (Apo) B/ApoA-1 ratio and smoking are the most important RFs.[47] Low education level is associated with increased risk of acute MI worldwide.

Diet. Consumption of green leafy vegetables and fruits could play a role in the reduction in the risk of CAD.[46] Despite the fact that nearly half of SAs are lifelong vegetarians, the rates of DM and CAD are as high as in nonvegetarians. The use of saturated fat acids (SAFAs) and/or trans-unsaturated fatty acids (TRUFAs) among SAs is very common. Whole milk, clarified butter (ghee), and deep frying are used for many SA dishes.[53] As SA people used to prepare vegetables with plenty amounts of SAFA and TRUFA, the levels of lipoprotein remain the same among SA vegetarians and nonvegetarians.[19,53,54] Moreover, TRUFA that is formed by the partial hydrogenation of cooking vegetable oils increases LDL-C and decreases HDL-C leading to a greater TC–HDL-C ratio.[55,56] Recent data indicate that very low amount of fat and very high carbohydrate diet would result in worsening of dyslipidemia in terms of increased TG and decreased HDL-C levels.[57] Protective lifestyle factors such as leisure time physical activity and regular intake of fruits and vegetables are markedly lower in some SA countries than Western populations.[46] Data from the INTERHEART study showed that the rates of fruits and vegetables consumption were lower in SA controls compared with controls from other areas, despite the higher rate of vegetarians among Indians.[46] However, in Bangladesh, that has the youngest age of AMI occurrence, the rate of fruit and vegetable consumption is lowest among SAs. Furthermore, even in those who use fruits and vegetables, the expected benefits are suboptimal. This could be explained in part by the destruction of 90% of folate content through the common habit of prolonged cooking of vegetables in SAs. The inverse association between vegetable consumption and occurrence of AMI has been reported in a case–control study from India.[46]

Smoking. The rates of smoking in SA men are lower than in Japan, China, and other Asian countries and are very low in SA women.[58] However, smoking is common among Bangladeshi men.[59]

Alcohol consumption. Joshi et al found that alcohol consumption was not associated with AMI in SAs; however, among Indians, there was a significant unfavorable link between alcohol consumption and AMI.[46] Moreover, the authors reported that alcohol consumption did not appear to be protective in native SAs and this was related to the lower prevalence or differences in patterns of drinking. Also, it has been noted that alcohol consumption was very low in the SA countries in which the majority of population are Muslims.

Metabolic syndrome. The definition of the metabolic syndrome has been revised for Asian Indians in a recent report.[60] Also, data show that metabolic syndrome and its CV burden in SAs is high and starts at an early age.[60]

As a characteristic feature of the SA population, the proportion of body fat is high and centrally distributed.[61] A natural tendency toward central obesity is an established RF that may lead to a higher incidence of CAD among SAs through its effects on blood pressure, DM, and insulin resistance.[62-64] Prevalence of DM, hyperinsulinemia, and insulin resistance is high in SAs that are known RFs for CAD.[16,54,65] Insulin resistance also independently increases the risk of CAD either directly or through its impact on lipid metabolism.[66] The cause of the increased prevalence of insulin resistance and DM among SAs is unclear.[67]

Wild et al reported more than one-sixth of cases of DM reside in India, which ranks first among all SA countries in the number of patients with DM.[68] Notably, SAs living abroad develop DM at an earlier age than caucasians.[69] Moreover, SAs have a higher prevalence of IGT and increased levels of fasting glucose.[14,70]

Lipid Profile. The lipid profile of SAs is characterized by high total cholesterol–HDL-C ratio and high levels of small dense fraction of LDL, which is highly atherogenic.[71,72]

The link between low HDL-C level and the risk of CAD is related to the ability of HDL-C to enhance cholesterol ester and TG metabolism.[73] Prior data showed an inverse relationship between HDL-C and endogenous tissue plasminogen activator inhibitor 1 (PAI-1) and so its favorable effect may be mediated in part through alterations in fibrinolytic activity.[73] In general, low HDL-C levels are reported in SAs which has been mainly attributed to their dietary habits.[17,64,71-73]

The cardioprotective effect of HDL-C is mainly related to larger HDL-C particles.[74] A comparison with the Framingham Offspring Study revealed lower concentrations of large HDL-C and significantly higher concentrations of small HDL-C among SA men.[75] South Asians have a smaller LDL size than either caucasians or East Asians.[76] Increased levels of small dense LDL (sdLDL) is a feature of very high CV risk.[77] Also, sdLDL could be a marker for the diagnosis and severity of the metabolic syndrome.[77,78]

Nonconventional (Emerging) RFs. Data on the conventional CV RFs do not clearly explain the high risk of CAD among SAs.[79] The Southall and Brent prospective follow-up studies showed that higher CAD mortality was seen in SAs compared with

European men. Moreover, the mortality rate was about 60% higher in SAs and the conventional RFs failed to explain this mortality difference.[79] Therefore, further studies are needed to generate evidence on nonconventional RFs.[80]

Dysfunctional HDL

Evidence suggests that not only the level of HDL-C but also its functionality plays a role in the development of CAD.[80] South Asians not only have low levels of HDL-C but also have a high prevalence of proinflammatory dysfunctional HDL-C which inhibits the antioxidant properties of HDL-C and promotes the formation of LDL-derived oxidized lipids.[80,81] The prevalence of dysfunctional HDL-C was reported in a single study as around 50% of the SAs participants.[80] Unfortunately, data on the role of medications that could improve HDL-C dysfunction are not definitive.[82]

C-Reactive protein

C-Reactive protein (CRP), in the arterial wall, forms aggregates that bind and cluster LDL molecules that eventually triggers the atherosclerotic process.[83-85] C-Reactive protein is also associated with plaque vulnerability in patients with CAD.[84,86] Studies conducted in SAs showed positive association between elevated CRP and CAD.[83] According to Chambers et al, CRP levels were considerably higher in SAs than in Europeans, and this was mainly attributed to the high prevalence of abdominal obesity and insulin resistance in SAs.[87] Experimental studies suggest that abdominal adipose tissue is a major source of cytokines, including interleukin 6, which in turn is a determinant of hepatic CRP synthesis.[88] Thus, high prevalence of central obesity in SAs may contribute to increased CAD risk in SAs through inflammatory mechanisms, the action being mediated by CRP.[87] On the other hand, limited data found a moderate association between CRP and CAD.[89]

Thrombogenic RFs

Several studies showed that SAs are characterized by high plasma levels of fibrinogen,[90] PAI-1,[91,92] lipoprotein(a), Lp(a)[14,91], homocysteine,[93,94] and enhanced platelet activity[95] in addition to decreased endogenous fibrinolytic activity.[92,96]

Lipoprotein(a). Lipoprotein(a) is an emerging independent RF for the development of CAD and thought to augment the effect of conventional RFs such as low HDL-C, high LDL-C, and DM.[97,98]

Unlike other lipids, the serum levels of Lp(a) are determined mainly by genetic background.[97] Based on that, the high levels of Lp(a) in SAs may explain some of the increased CAD risk in these ethnic groups.[97]

As the Lp(a) associated CAD risk is highest between 45 and 55 years of age and declines in old age, some data recommended screening for Lp(a) in younger SAs.[7,99] South Asians have a higher CAD risk at any given level of LDL-C and total cholesterol because of the multiplicative effect of Lp(a) on other CAD RFs. Physicians should be aware that this leads to a significant underestimation of CAD risk in SAs by the Framingham risk score.[97]

Bhatnagar et al concluded that serum Lp(a) levels were similar between SAs immigrants in the United Kingdom and their siblings in India, but were significantly higher than those of white European populations there.[41]

The Study of Health Assessment and Risk in Ethnic Groups (SHARE) identified Lp(a) and PAI-1 as independent RFs of CAD among the SA population.[14]

Lipoprotein(a) acts as a link between atherosclerosis and thrombosis and its atherogenicity was found to be 10-fold higher than LDL-C. Moreover, Lp(a) has high thrombogenic and antifibrinolytic properties.[100]

The Regression Growth Evaluation Statin Study (REGRESS) group reported that the pathophysiological effects of Lp(a) are exponentially increased by concomitant low HDL-C.[101]

Homocysteine. Homocysteine has been considered as an emerging RF for CAD in Indians.[93,102] Higher homocysteine levels are found among SA compared with whites in several countries.[93,94] The deficiency in folate or vitamin B12 may explain the difference in homocysteine levels between SAs and other ethnicities.[51,103] Adherence to strict vegetarian diets or prolonged cooking of vegetables among SA households was implicated in vitamin B_{12} and folate deficiency in this population.[51,103] Refsum et al[104] reported that Indians have a very high prevalence of hyperhomocystinemia, which was strongly correlated with impaired cobalamin status more than folate deficiency. Few studies showed no relationship of homocysteine with CAD in India; however, these studies had small sample size.[39]

Platelet size and function. The impact of platelet size and function is another potential RF.[73] Previous studies and a meta-analysis suggest a correlation between large platelets and high mean platelet volume (MPV) and the risk of thrombosis.[105] High MPV is associated with a couple of established RFs such as DM and dyslipidemia, CV disorders, low-grade inflammatory conditions, and tendency for development of arterial and venous thrombosis.[105]

The Chennai Urban Population Study (CUPS) showed increased platelet activity in patients with CAD and DM after controlling for other RFs and independent of each other.[70] However, the level of risk attributed to increased platelet activity on SAs compared with other communities remains understudied.

Inflammation

Inflammation in terms of high-sensitivity CRP (hsCRP) and adipose tissue-derived circulating hormones plays a role in the development and progression of atherosclerosis.[106-109] There are many proinflammatory adipokines such as tumor necrosis factor α, interleukin 6, leptin, PAI-1, angiotensinogen, resistin, and hsCRP. Adipose tissue is the source of anti-inflammatory

and antiatherosclerotic adipokines such as adiponectin.[109-112] Previous reports from SA populations demonstrated that altered adipokine production or action may play a role in the heightened CV disease risk. Raji et al showed lower adiponectin levels among SAs when compared with whites, which paralleled increased insulin resistance, impaired fibrinolysis, and altered endothelial function in this population.[113] Low adiponectin levels in nondiabetic SAs may not only reflect increased CV disease risk but also may be linked to the development of DM in SAs.[114] Moreover, change in levels of adipokines may explain decreased insulin sensitivity among nondiabetic SAs when compared with whites and Chinese patients.

Microalbuminuria

Microalbuminuria is recognized as an independent CV disease RF.[115] A comparative study from the United Kingdom reported urinary albumin excretion is higher, and microalbuminuria is more frequent in SAs than in the overall population, even after adjustment for age, hypertension, and DM.[115] Furthermore, SA type 2 DM patients develop more nephropathy and have progressive renal failure in comparison with Dutch European patients.[116]

Telomere Length

A telomere is the region of repetitive nucleotide sequences at each end of a chromatid, which protects the end of the chromosome from deterioration or from fusion with neighboring chromosomes. Mean telomere length is recognized a marker of biological age primarily at the cellular level and shorter telomeres indicate increased biological age.[117,118] Patients having CAD with multiple-vessel disease tend to have shorter telomeres in comparison with healthy individuals with no CAD.[117] Mukherjee et al studied the association of telomere length with CAD in Indian individuals and concluded that telomere biology is altered in patients with CAD.[118] Indians with CAD have shorter telomeres than patients without such a history.[117]

Fetal Programming and Early Life Influences

According to Barker, nutrition of babies before birth and during infancy influences the development of RFs in terms of raised blood pressure, fibrinogen concentration, factor VIII concentration, and IGT and thus is a key determinant of CAD in later life.[119,120]

A recent prospective cohort study,[121] the New Delhi Birth Cohort, showed that the metabolic risk of CAD and other CV disease was higher in individuals who were born with a low birth weight but rapidly gained weight throughout childhood and adolescence. Furthermore, other studies from India and Bangladesh showed that fetal programming hypothesis as an RF for CV disease needs further confirmations before being generalizable.[122]

Smaller Mean Coronary Artery Diameter

Smaller mean coronary artery diameter has been proposed as an RF for CAD in SAs. Previous studies had shown smaller coronary artery diameters in SAs, but the trend was insignificant when corrected for body surface area.[123,124]

Makaryus et al studied those who had normal coronary angiogram and showed that, in comparison to whites, SAs had significantly smaller coronary artery diameters, even when corrected for body surface area.[125]

Smaller coronary arteries may require a lower atheroma burden to develop critical stenosis and that may lead to premature CAD.[123,124] Tillin et al[126] reported, in patients with CAD, that increased coronary artery stenosis, despite equivalent levels of calcified disease, in SAs is related to narrower arteries. Moreover, reduced coronary artery diameter is associated with advanced disease in Europeans but not in SAs, reflecting the ethnic differences in vascular remodeling.[126]

South Asian Women and CV RFs

Although both men and women have the same CV disease RFs, significant changes have been shown after menopause and estimated 70% of CV disease deaths are attributed to modifiable RFs.[127] Compared with males, the excess burden of heart disease among SA women worldwide was addressed in several studies.[7,9,128] Atherogenic dyslipidemia characterized by high TG and low HDL-C concentrations is highly prevalent among SA women and in turn related to insulin resistance.[129]

The CADI study showed that the prevalence and severity of CAD including 3-vessel disease was as high as 40% in Indian women and the majority of women were premenopausal.[10] The Canadian angiographic study reported that left main or 3-vessel CAD among SA women was twice compared with white women.[96] Despite the low rates of smoking among women in India (<10%), the overall heart disease rate is nearly as high as in men. Regular physical exercise is almost nonexistent in SA women due to cultural limitations.

In Singapore, CAD mortality among young SA women is 8-fold higher than Chinese women of the same age.[130] Similarly, CAD mortality reported was significantly higher among SA women in California.[131]

Are all SAs at Equivalent Risk

Variation in risk of CV disease among the Indian subcontinent population is evident in many studies.[132] Bangladeshis are at greatest risk of developing CAD, followed by Pakistanis and then Indians.[71] High prevalence of tobacco use like cigarettes and beedis was reported in Bangladeshi men. Even Bangladeshi women were reported with highest rates of CAD mortality in the United Kingdom.[133] Joshi et al evaluated the association of RFs for AMI in native younger SAs, compared with other countries.[46] The authors concluded that depression and stress at work or home are significantly associated with AMI among SAs. Bangladesh had the lowest prevalence for regular physical activity and daily intake of fruits and vegetables. However,

Bangladesh had the highest prevalence for the most RFs among the SAs in terms of smoking, elevated ApoB100–Apo-AI ratio, abdominal obesity, hypertension, and depression. Indians had the highest prevalence of DM in that study. South Asians have higher prevalence of DM compared with other ethnicities. This high prevalence is observed in SAs whether they migrate to the Western countries or live in their country of origin and being diagnosed at a younger age.[134]

Coronary Artery Disease RFs and the SA Paradox

Although the prevalence of CAD is high among SAs, many of the traditional CAD RFs such as smoking, hypertension, and obesity are not higher among SAs. Moreover, smoking is actually lower among SAs and almost nonexistent among SA females.[97] This was particularly true in the CADI study, which revealed a similar or lower prevalence of all major conventional RFs, except for DM.[10] The high rate of CAD among SAs points to the role of a genetic RF which may remain uncontrolled even with optimum modification of lifestyle.[39]

South Asians Response to Drugs Used in Patients With CAD

Data for the impact of SA ethnicity on the response to medications used for CV primary prevention are scarce. However, subanalysis of the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA) to compare statin efficacy among different ethnic groups showed that a standard dose of atorvastatin improved lipid profiles to a similar extent in whites, blacks, and SAs.[135] However, there was no significant effect of atorvastatin on HDL-C in any ethnic group. Recently, Brunner et al[136] evaluated the associations between statin use and outcomes in different ethnicities with DM. The authors concluded that statin use is associated with lower mortality in white, Chinese, and SAs with newly diagnosed DM.[136]

Antiplatelet drugs are important for prevention of CV disease. Previous data showed decreased response to clopidogrel among Asians due to genetic polymorphisms associated with clopidogrel resistance, which is around 70% in some of the Asian communities.[137]

The genetic factors that underlie varying responses to medicines observed among different ethnic groups have been studied. The prevalence of the CYP2D6 (acts on different β-blockers) poor metabolizer phenotype is around 2.0% in Asian populations.[138] Furthermore, ApoE exists in several polymorphic variants and affects disease progression and the action of drugs. The frequency of APoE polymorphisms varies among populations; it reaches 5% to 7% in Chinese populations and 10% in other Asian and American Indian groups.[139] These polymorphisms also appear to affect response to lipid-lowering drugs, including fibrates and statins, but the data are not clear.[138]

Limitations

This is a qualitative overview of the published literature, thus we are not able to weigh and pool estimates from the included articles. We also acknowledge that most studies included are from the Indian subcontinent, but this is mainly due to the limited availability of literature from other SA countries that fit the inclusion criteria. We realize that the RFs identified in these studies may be influenced by several cultural differences, socioeconomic attributes, and the differences in the environment among the SA countries and therefore may not be easily generalized from one SA group to another. There are across- and within-country differences in cultural factors among the different population groups and these cultural differences and their role in modulating the effects of the conventional and emerging RFs need to be further addressed.

Conclusions

Despite the number of studies published, there is no definitive evidence that SA origin can be used as an independent RF when considering a patient's CAD risk in order to plan interventions. SAs have higher rates and earlier onset of CAD due to various predisposition and lifestyle factors. Although the conventional RFs do not fully explain the excess burden of CAD, these RFs are important in SAs and remain the principal targets for prevention and treatment. Due to potential genetic susceptibility, the adverse effects of the conventional RFs are magnified several fold. Thorough CV risk assessment and modification, especially at younger ages, should be considered in all SAs.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Bhopal RS. *Ethnicity, Race and Health in Multicultural Societies: Foundations for Better Epidemiology, Public Health and Healthcare*. Oxford: Oxford University Press; 2007.
2. Rambihar VS, Rambihar SP, Rambihar VS. Race, ethnicity, and heart disease: a challenge for cardiology for the 21st century. *Am Heart J*. 2010;159(1):1-14.
3. Rambihar VS, Rambihar S, Rambihar V. South Asian heart: the simple and the complex. In: *Tsunami Chaos and Global Heart: Using Complexity Science to Rethink and Make a Better World*. Toronto: Vashna Publications; 2005:137-151. http://www.femmefractal.com/tsunami.htm. Accessed August 1, 2009.
4. Peterson E, Yancey CW. Eliminating racial and ethnic disparities in cardiac care. *N Engl J Med*. 2009; 360(12):1172-1174.
5. Reddy KS. Ethnic diversity: the new challenge of preventive cardiology. *J Int Soc Fed Cardiol*.1998;1(1):6-8.

6. Enas EA. Coronary artery disease epidemic in Indians: a cause for alarm and call for action. *J Indian Med Assoc*. 2000;98(11): 694-703.
7. Danarag TJ, Acker M, Danaraj W, Ong W, Yam T. Ethnic group differences in coronary heart disease in Singapore: an analysis of necropsy records. *Am Heart J*. 1959;58(4):516-526.
8. Enas EA, Senthilkumar A, Juturu V, Gupta R. Coronary artery disease in women. *Indian Heart J*. 2001;53(3):282-292.
9. Dave TH, Wasir HS, Prabhakaran D, et al. Profile of coronary artery disease in Indian women: Correlation of clinical, non invasive and coronary angiographic findings. *Indian Heart J*. 1991; 43(1):25-29.
10. Enas EA, Mehta J. Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention and therapy. Coronary Artery Disease in Asian Indians (CADI) Study. *Clin Cardiol*. 1995;18(3):131-135.
11. Zimmerman FH, Cameron A, Fisher L, Ng G. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). *J Am Coll Cardiol*. 1995;26(3):654-661.
12. Sharma SN, Kaul U, Sharma S, et al. Coronary arteriographic profile in young and old Indian patients with ischaemic heart disease: a comparative study. *Indian Heart J*. 1990; 42(5):365-369.
13. Pahlajani DB, Chawla MH, Kapashi KA. Coronary artery disease pattern in the young. *J Assoc Physicians India*. 1989;37(5): 312-314.
14. Anand SS, Yusuf S, Vuksan V, et al. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the study of health assessment and risk in ethnic groups (SHARE). *Lancet*. 2000;356(9226):279-284.
15. Kathuria N, Koenig K, Schwartzbard A, Mele KA. Accelerated atherosclerosis in South Asian expatriates living in New York City. *J Investig Med*. 1996; 44(3):312a.
16. Saleheen D, Frossard P. CAD risk factors and acute myocardial infarction in Pakistan. *Acta Cardiol*. 2004;59(4):417-424.
17. Reddy KS, Prabhakaran D, Jeemon P, et al. Educational status and cardiovascular risk profile in Indians. *Proc Natl Acad Sci U S A*. 2007;104(41):16263-16268.
18. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*.1998;97(6):596-601.
19. Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Indian Heart J*. 1996;48(4):343-353.
20. Enas EA. Avoiding premature coronary deaths in British asians: guidelines for pharmacologic intervention are needed. *BMJ*. 1996;312(7027):376.
21. Rajadurai J, Arokiasami J, Pasamanichan K, Shatar A, Mei-Lin O. Coronary disease in Asians. *Aus N Z J Med*. 1992;22(4):345-348.
22. Bahuleyan CG. Hospital data on coronary heart disease from North Kerala. In: Vijayaraghavan G, ed. *Cardiovascular Disease Prevention*. Thiruvananthapuram, Kerala: Trivandrum Medical College; 1996:54-59.
23. Negus BH, Willard JE, Glamann DB, et al. Coronary anatomy and prognosis of young, asymptomatic survivors of myocardial infarction. *Am J Med*. 1994;96(4):354-358.
24. Hughes LO, Raval U, Raftery E. First myocardial infarctions in Asian and White men. *BMJ*. 1989;298(6684):1345-1350.
25. Enas EA, Dhawan J, Petkar S. Coronary artery disease in Asian Indians: lessons learnt and the role of lipoprotein (a). *Indian Heart J*. 1997;49(1):25-34.
26. Balarajan R. Ethnic differences in mortality from ischaemic heart disease and cerebrovascular disease in England and Wales. *BMJ*. 1991;302(6776):560-564.
27. Reddy KS. Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. *Public Health Nutr*. 2002;5(1A):231-237.
28. Office of the Registrar General and Census Commissioner India. *Population Projections for India and States 2001e2026*. New Delhi, India: Report of the Technical Group on Population Projections Constituted by the National Commission on Population; 2006.
29. Patel V, Chatterji S, Chisholm D, et al. Chronic diseases and injuries in India. *Lancet*. 2011;377(9763):413-248.
30. Ng E. The healthy immigrant effect and mortality rates. *Health Rep*. 2011;22(4):25-29.
31. Lassetter JH, Callister LC. The impact of migration on the health of voluntary migrants in western societies. *J Transcult Nurs*. 2009;20(1):93-104.
32. Lear SA, Humphries KH, Hage-Moussa S, Chockalingam A, Mancini GB. Immigration presents a potential increased risk for atherosclerosis. *Atherosclerosis*. 2009;205(2):584-589.
33. Mooteri SN, Petersen F, Dagubati R, Pai RG. Duration of residence in the United States as a new risk factor for coronary artery disease (The Konkani Heart Study). *Am J Cardiol*. 2004;93(3): 359-361.
34. Diez Roux AV, Detrano R, Jackson S, et al. Acculturation and socioeconomic position as predictors of coronary calcification in a multiethnic sample. *Circulation*. 2005;112(11):1557-1565.
35. Choi S, Rankin S, Stewart A, Oka R. Effects of acculturation on smoking behavior in Asian Americans: a meta-analysis. *J Cardiovasc Nurs*. 2008;23(1):67-73.
36. Sheth T, Nair C, Nargundkar M, Anand S, Yusuf S. Cardiovascular and cancer mortality among Canadians of European, South Asian and Chinese origin from 1979 to 1993: an analysis of 1.2 million deaths. *Can Med Assoc J*. 1999;161(2):132-138.
37. Gupta R, Gupta R, Agrawal A, et al. Migrating husbands and changing cardiovascular risk factors in the wife: a cross sectional study in Asian Indian women. *J Epidemiol Community Health*. 2012;66(10):881-889.
38. Padmavati S.Epidemiology of cardiovascular disease in India. II. Ischemic heart disease. *Circulation*.1962;25(4):711-717.
39. Enas EA, Senthilkumar A. Coronary artery disease in Asian Indians: an update and review. *Internet J Cardiol*. 2000;1(2):2.
40. Ebrahim S, Kinra S, Bowen L, et al. The effect of rural-to-urban migration on obesity and diabetes in India: a cross sectional study. *PLoS Med*. 2010;7(4):e1000268.
41. Bhatnagar D, Anand IS, Durrington PN, et al. Coronary risk factors in people from the Indian subcontinent living in west London and their siblings in India. *Lancet*. 1995;345(8947):405-409.
42. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part II: variations in cardiovascular disease by

specific ethnic groups and geographic regions and prevention strategies. *Circulation*. 2001;104(23):2855-2864.
43. Gupta M, Singh N, Verma S. South Asians and cardiovascular risk: what clinicians should know? *Circulation*. 2006;113(25):e924-e929.
44. Enas EA, Singh V, Munjal YP, Bhandari S, Yadave RD, Manchanda SC. Reducing the burden of coronary artery disease in India: challenges and opportunities. *Indian Heart J*. 2008;60(2): 161-175.
45. Yeo KK, Tai BC, Heng D, et al. Ethnicity modifies the association between diabetes mellitus and ischaemic heart disease in Chinese, Malays and Asian Indians living in Singapore. *Diabetologia*. 2006;49(12):2866-2873.
46. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA*. 2007;297(3):286-294.
47. Yusuf S, Hawken S, Ounpuu S, et al. INTERHEART Investigators effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364(9438):937-952.
48. Muir CS. Coronary heart disease in seven racial groups in Singapore. *British Heart J*. 1960;22(1):45-53.
49. Wattley GH. Myocardial infarction in South Trinidad. *WI Med J*. 1959;8:33-36.
50. Shaper AG, Jones KW. Serum cholesterol, diet and coronary heart disease in Africans and Asians in Uganda. *Lancet*. 1959;2(7102): 534-537.
51. Rambihar VS, Jagdeo DG. Ethnocultural heart: another challenge for an emerging diversity. *Can J Cardiol*. 1995;11(5):441-442.
52. Ajay VS, Prabhakaran D. Coronary heart disease in Indians: implications of the INTERHEART study. *Indian J Med Res*. 2010;132(5):561-566.
53. Yagalla MV, Hoerr S, Song W, Enas E, Garg A. Relationship of diet, abdominal obesity, and physical activity to plasma lipoprotein levels in Asian Indian physicians residing in the United States. *J Am Dietetic Assoc*. 1996;96(3):257-261.
54. Kris-Etherton P, Daniels SR, Eckel RH, et al. Summary of the scientific conference on dietary fatty acids and cardiovascular health: conference summary from the nutrition committee of the American heart association. *Circulation*. 2001;103(7):1034-1039.
55. Enas EA. Cooking oil, cholesterol and coronary artery disease. *Indian Heart J*. 1996;48(4):423-427.
56. Ascherio A, Hennekens C, Buring J, Master C, Stampfer M, Willett W. Trans-fatty acids and risk of myocardial infarction. *Circulation*. 1994;89(1):94-101.
57. Abbasi F, McLaughlin T, Lamendola C, et al. High carbohydrate diets, triglyceride-rich lipoproteins, and coronary heart disease risk. *Am J Cardiol*. 2000;85(1):45-48.
58. Enas EA. Cardiovascular diseases in Asian Americans and Pacific Islanders. *Asian Am Pac Islander J Health*. 1996;4(1-3):119-120
59. Bhopal R, Unwin N, White M, et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, and European origin populations: cross sectional study. *BMJ*. 1999; 319(7204):215-220.
60. Misra A, Khurana L. The metabolic syndrome in South Asians: epidemiology, determinants, and prevention. *Metab Syndr Relat Disord*. 2009;7(6):497-514.
61. Sniderman AD, Bhopal R, Prabhakaran D, Sarrafzadegan N, Tchernof A. Why might South Asians be so susceptible to central obesity and its atherogenic consequences? The adipose tissue overflow hypothesis. *Int J Epidemiol*. 2007;36(1): 220-225.
62. Snehalatha C, Ramachandran A, Saltyamurthy I, et al. Association of proinsulin and insulin resistance with coronary artery disease in nondiabetic south Indian men. *Diabet Med*. 2001;18(9): 706-708.
63. Venkatramana P, Reddy PC. Association of overall and abdominal obesity with coronary heart disease risk factors: comparison between urban and rural Indian men. *Asia Pac J Clin Nutr*. 2002;11(1):66-71.
64. Prabhakaran D, Shah P, Chaturvedi V, Ramakrishnan L, Manhapra A, Reddy KS. Cardiovascular risk factor prevalence among men in a large industry of North India. *Natl Med J India*. 2005; 18(2):59-65.
65. Deepa R, Mohan V, Premanand C, et al. Accelerated platelet activation in Asian Indians with diabetes and coronary artery disease: the Chennai urban population study (CUPS-13). *J Assoc Physicians India*. 2006;54(2):704-708.
66. Mohan V, Deepa M, Farooq S, Prabhakaran D, Reddy KS. Surveillance for risk factors of cardiovascular disease among an industrial population in southern India. *Natl Med J India*. 2008; 21(1):8-13.
67. Tziomalos K, Weerasinghe CN, Mikhailidis DP, Seifalian AM. Vascular risk factors in South Asians. *Int J Cardiol*. 2008; 128(1):5-16.
68. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of Diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-1053.
69. Mukhopadhyay B, Forouhi NG, Fisher BM, Kesson CM, Sattar N. A comparison of glycaemic and metabolic control over time among South Asian and European patients with Type 2 diabetes: results from follow-up in a routine diabetes clinic. *Diabet Med*. 2006;23(1):94-98.
70. Gerstein HC, Anand S, Yi QL, et al. The relationship between dysglycemia and atherosclerosis in South Asian, Chinese, and European individuals in Canada: a randomly sampled cross-sectional study. *Diabetes Care*. 2003;26(1):144-149.
71. Gama R, Elfatih AB, Anderson NR. Ethnic differences in total and HDL cholesterol concentrations: Caucasians compared with predominantly Punjabi Sikh Indo-Asians. *Ann Clin Biochem*. 2002;39(6):609-611.
72. Kulkarni KR, Markovitz JH, Nanda NC, Segrest JP. Increased prevalence of smaller and denser LDL particles in Asian Indians. *Atheroscler Thromb Vasc Biol*. 1999;19(11):2749-2755.
73. Ridker PM, Antman EM. Pathogenesis and pathology of coronary heart disease syndromes. *J Thromb Thrombolysis*. 1999;8(3): 167-189.
74. Johansson J, Carlson LA, Landou C, Hamsten A. High-density lipoproteins and coronary atherosclerosis. A strong inverse relation with the largest particles is confined to normotriglyceridemic patients. *Arterioscler Thromb*. 1991;11(11):174-182.
75. Bhalodkar NC, Blum S, Rana T, et al. Comparison of levels of large and small high-density lipoprotein cholesterol in Asian

Indian men compared with Caucasian men in the Framingham offspring study. *Am J Cardiol*. 2004;94(12):1561-1563.
76. Raschke V, Elmadfa I, Bermingham MA, Steinbeck K. Low density lipoprotein subclasses in Asian and Caucasian adolescent boys. *Asia Pac J Clin Nutr*. 2006;15(4):496-501.
77. Mikhailidis DP, Elisaf M, Rizzo M, et al. "European panel on low density lipoprotein (LDL) subclasses": a statement on the pathophysiology, atherogenicity and clinical significance of LDL subclasses: executive summary. *Curr Vasc Pharmacol*. 2011;9(5): 531-532.
78. Mikhailidis DP, Elisaf M, Rizzo M, et al. "European panel on low density lipoprotein (LDL) subclasses": a statement on the pathophysiology, atherogenicity and clinical significance of LDL subclasses. *Curr Vasc Pharmacol*. 2011;9(5):533-571.
79. Forouhi NG, Sattar N, Tillin T, McKeigue PM, Chaturvedi N. Do known risk factors explain the higher coronary heart disease mortality in South Asian compared with European men? Prospective follow-up of the Southall and Brent studies, UK. *Diabetologia*. 2006;49(11):2580-2588.
80. Dodani S, Kaur R, Reddy S, Reed GL, Navab M, George V. Can dysfunctional HDL explain high coronary artery disease risk in South Asians? *Int J Cardiol*. 2008;129(1):125-132.
81. Dodani S, Marion L, Sharma G, Reed GL, George V. The association of carotid intima media thickness with dysfunctional HDL in South Asians. *Arch Med Sci*. 2008;4(1):40-46.
82. Otocka-Kmiecik A, Mikhailidis DP, Nicholls SJ, Davidson M, Rysz J, Banach M. Dysfunctional HDL: a novel important diagnostic and therapeutic target in cardiovascular disease? *Prog Lipid Res*. 2012;51(4):314-324.
83. Mohan V, Deepa R, Velmurugan K, Premalatha G. Association of C-reactive protein with body fat, diabetes and coronary artery disease in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-6). *Diabet Med*. 2005;22(7):863-870.
84. Fu T, Borensztajn J. Macrophage uptake of low-density lipoprotein bound to aggregated C-reactive protein: possible mechanism of foam-cell formation in atherosclerotic lesions. *Biochem J*. 2002;366(1):195-201.
85. Patel JV, Dwivedi S, Hughes EA, Lip GY. Premature coronary artery disease: An inferred cardiovascular variant or a South Asian genetic disorder? *Thromb Haemost*. 2008;99(6): 991-992.
86. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *N Engl J Med*. 2000;342(12): 836-843.
87. Chambers JC, Eda S, Bassett P, et al. C-reactive protein, insulin resistance, central obesity, and coronary heart disease risk in Indian Asians from the United Kingdom compared with European whites. *Circulation*. 2001;104(2):145-150.
88. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol*. 1999;19(4):972-878.
89. Danesh J, Wheeler JG, Hirschfield GM, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *N Engl J Med*. 2004;350(14): 1387-1397.
90. Mazer SP, Rabbani LE. Evidence for C-reactive protein's role in (CRP) vascular disease: atherothrombosis, immuno-regulation and CRP. *J Thromb Thrombolys*. 2004;17(2):95-105.
91. Bainey KR, Jugdutt BI. Increased burden of coronary artery disease in South-Asians living in North America. Need for an aggressive management algorithm. *Atherosclerosis*. 2009;204(1):1-10.
92. Bedi US, Singh S, Syed A, Aryafar H, Arora R. Coronary artery disease in South Asians: an emerging risk group. *Cardiol Rev*. 2006;14(2):74-80.
93. Chambers JC, Obeid OA, Refsum H, et al. Plasma homocysteine concentrations and risk of coronary heart disease in UK Indian Asian and European men. *Lancet*. 2000;355(9203):523-527.
94. Hughes K, Ong CN. Homocysteine, folate, vitamin B12, and cardiovascular risk in Indians, Malays, and Chinese in Singapore. *J Epidemiol Community Health*. 2000;54(1):31-34.
95. Markovitz JH, Kulkarni K, Goldschmidt-Clermont P, et al. Increased platelet activation and fibrinogen in Asian Indians. Potential implications for coronary risk. *Eur Heart J*. 1998; 19(5):720-726.
96. Gupta M, Brister S. Is South Asian ethnicity an independent cardiovascular risk factor? *Can J Cardiol*. 2006;22(3):193-197.
97. Coronary artery disease in south Asians, (2009). http://www.clinicalcorrelations.org/?p=1023. Accessed April 24, 2014.
98. Enas EA. Clinical implications: dyslipidemia in the Asian Indian Population. https://southasianheartcenter.org/docs/AAPImonograph.pdf. Accessed 24 April 2014.
99. Enas EA, Chacko V, Pazhoor SG, Chennikkara H, Devarapalli P. Dyslipidemia in South Asian Patients. *Curr Atherosclerosis Rep*. 2007;9(5):367-374.
100. Scanu AM.Lipoprotein (a): A genetically determined cardiovascular pathogen in search of a function. *J Lab Clin Med*. 1990; 116(2):142-146.
101. Cobbaert C, Jukema JW, Zwinderman AH, Withagen AJ, Lindemans J, Bruschke AV. Modulation of lipoprotein (a) atherogenicity by high density lipoprotein cholesterol levels in middle-aged men with symptomatic coronary artery disease and normal to moderately elevated serum cholesterol. Regression growth evaluation statin study (REGRESS) study group. *J Am Coll Cardiol*. 1997;30(6):1491-1499.
102. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: Probable benefits of increasing folic acid intakes. *JAMA*.1995;274(13):1049-1057.
103. Chambers JC, Ireland H, Thompson E, et al. Methylenetetrahydrofolate reductase 677 C→T mutation and coronary heart disease risk in UK Indian Asians. *Arterioscler Thromb Vasc Biol*. 2000;20(11):2448-2452.
104. Refsum H, Yajnik CS, Gadkari M, et al. Hyperhomocysteinemia and elevated methylmalonic acid indicate a high prevalence of cobalamin deficiency in Asian Indians. *Am J Clin Nutr*. 2001; 74(2):233-241.
105. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;17(1):47-58.

106. Szmitko PE, Wang CH, Weisel RD, de Almeida JR, Anderson TJ, Verma S. New markers of inflammation and endothelial cell activation: part I. *Circulation*. 2003;108(16):1917-1923.
107. Szmitko PE, Wang CH, Weisel RD, Jeffries GA, Anderson TJ, Verma S. Biomarkers of vascular disease linking inflammation to endothelial activation: part II. *Circulation*. 2003;108(17): 2041-2048.
108. Verma S, Szmitko PE, Ridker PM. C-reactive protein comes of age. *Nat Clin Pract Cardiovasc Med*. 2005;2(1):29-36.
109. Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atherosclerosis. *Am J Physiol Heart Circ Physiol*. 2005;288(5):H2031-H2041.
110. Verma S, Li SH, Wang CH, et al. Resistin promotes endothelial cell activation: further evidence of adipokine-endothelial interaction. *Circulation*. 2003;108(6):736-740.
111. Shibata R, Sato K, Pimentel DR, et al. Adiponectin protects against myocardial ischemia-reperfusion injury through AMPK- and COX-2-dependent mechanisms. *Nat Med*. 2005;11(10): 1096-1103.
112. Despres JP, Golay A, Sjostrom L; Rimonabant in obesity-lipids study group. Effects of rimonabant on metabolic risk factors in overweight patients with dyslipidemia. *N Engl J Med*. 2005; 353(20):2121-2134.
113. Raji A, Gerhard-Herman MD, Warren M, et al. Insulin resistance and vascular dysfunction in nondiabetic Asian Indians. *J Clin Endocrinol Metab*. 2004;89(8):3965-3972.
114. Snehalatha C, Mukesh B, Simon M, Viswanathan V, Haffner SM, Ramachandran A. Plasma adiponectin is an independent predictor of type 2 diabetes in Asian Indians. *Diabetes Care*. 2003;26(12):3226-3322.
115. Fischbacher CM, Bhopal R, Rutter MK, et al. Microalbuminuria is more frequent in South Asian than in European origin populations: a comparative study in Newcastle, UK. *Diabet Med*. 2003; 20(1):31-36.
116. Chandie Shaw PK, Baboe F, van Es LA, et al. South-Asian Type 2 diabetic patients have higher incidence and faster progression of renal disease compared with Dutch- European diabetic patients. *Diabetes Care*. 2006;29(6):1383-1355.
117. Samani NJ, Boultby R, Butler R, Thompson JR, Goodall AH. Telomere shortening in atherosclerosis. *Lancet*. 2001; 358(9280):472-473.
118. Mukherjee M, Brouilette S, Stevens S, Shetty KR, Samani NJ. Association of shorter telomeres with coronary artery disease in Indian subjects. *Heart*. 2009;95(8):669-673.
119. Barker DJP. Fetal and infant origins of adult disease. London: BMJ Publishing Group; 1992.
120. Barker DJP.Mothers, Babies, and disease in later life. London: BMJ Publishing Group; 1994.
121. Fall CH, Sachdev HS, Osmond C, et al. Adult metabolic syndrome and impaired glucose tolerance are associated with different patterns of BMI gain during infancy: data from the New Delhi Birth Cohort. *Diabetes Care*. 2008;31(12): 2349-2356.
122. Connor NE. Impact of fetal and neonatal malnutrition on the onset of puberty and associated noncommunicable disease risks. *Adolesc Health Med Therapeut*. 2011;2(1):15-25.
123. Lip GY, Rathore VS, Katira R, Watson RD, Singh SP. Do Indo-Asians have smaller coronary arteries? *Postgrad Med J*. 1999; 75(886):463-466.
124. Dhawan J, Bray CL. Are Asian coronary arteries smaller than Caucasian? A study on angiographic coronary artery size estimation during life. *Int J Cardiol*. 1995;49(3):267-269.
125. Makaryus AN, Dhama B, Raince J, et al. Coronary artery diameter as a risk factor for acute coronary syndromes in Asian-Indians. *Am J Cardiol*. 2005;96(6):778-780.
126. Tillin T, Dhutia H, Chambers J, et al. South Asian men have different patterns of coronary artery disease when compared with European men. *Int J Cardiol*. 2008;129(3):406-413.
127. Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women-2011 update a guideline from the American heart association. *J Am Coll Cardiol*. 2011;57(12):1404-1423.
128. Barnett AH, Dixon AN, Bellary S, et al. Type 2 diabetes and cardiovascular risk in the UK south Asian community. *Diabetologia*. 2006;49(10):2234-2246.
129. Palaniappan LP, Kwan AC, Abbasi F, Lamendola C, McLaughlin TL, Reaven GM. Lipoprotein abnormalities are associated with insulin resistance in South Asian Indian women. *Metabolism*. 2007;56(7):899-904.
130. Hughes K, Yeo PP, Lun KC, et al. Cardiovascular diseases in Chinese, Malays, and Indians in Singapore. II. Differences in risk factor levels. *J Epidemiol Community Health*. 1990;44(1): 29-35.
131. Palaniappan L, Wang Y, Fortmann SP. Coronary heart disease mortality for six ethnic groups in California, 1990-2000. *Ann Epidemiol*. 2004;14(7):499-506.
132. Garg PR, Kabita S, Singh HS, et al. Differences in conventional cardiovascular risk factors in two ethnic groups in India. *Ethn Dis*. 2012;22(3):372-376.
133. Shaw M, Dorling D, Gordon D, Davey Smith G. The widening gap: health inequalities and policy in Britain. Bristol: Policy Press, 1999.
134. Mitra AR, Irvin J. Diabetes in South Asians: etiology and the complexities of care. *Univ Br Columbia Med J*. 2010;2(1):20-23.
135. Chapman N, Chang CL, Caulfield M, et al. Ethnic variations in lipid-lowering in response to a statin (EVIREST): a substudy of the Anglo-scandinavian cardiac outcomes trial (ASCOT). *Ethn Dis*. 2011;21(2):150-157.
136. Brunner NW, Ramanathan K, Wang H, Quan H, Khan NA. Effectiveness of statin prescribing on reducing mortality in South Asian, Chinese, and White patients with diabetes. *Can J Cardiol*. 2013;29(8):920-926.
137. Hasan MS, Basri HB, Hin LP, Stanslas J. Genetic polymorphisms and drug interactions leading to clopidogrel resistance: why the Asian population requires special attention. *Int J Neurosci*. 2013;123(3):143-154.
138. Burroughs VJ, Maxey RW, Levy RA. Racial and ethnic differences in response to medicines: towards individualized pharmaceutical treatment. *J Natl Med Assoc*. 2002;94(10 suppl):1-26.
139. Siest G, Bertrand P, Herbeth B, et al. Apolipoprotein E polymorphisms and concentration in chronic diseases and drug responses. *Clin Chem Lab Med*. 2000;38(9):841-852.