

Coronary Heart Disease in South-Asian Women

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ABSTRACT

With the demographic transition in the South-Asian region coronary heart disease in post menopausal women is a major challenge. Women with myocardial infarction often have atypical presentation and have a higher mortality. In South-Asia there is high prevalence of coronary heart disease among women and there is an increasing incidence in both urban and rural areas. While obesity and lack of exercise contribute largely to traditional risk factors in South-Asian women in midlife, nontraditional newer risk factors seem to play a major role in increased prevalence and mortality. Early prevention strategies targeting diet, physical exercise and mental stress are important in preventing further increase of coronary heart disease in South-Asian women.

Keywords: Coronary heart disease, South-Asian women, Predisposition, Prevalence, Risk factors.

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INTRODUCTION

South Asia is home to over one-fifth of the world population, with three countries among the top ten most populated countries in the world. It is projected that, in 2030, the most populous country will be in South Asia. There are about 130 million postmenopausal women in the region and this is expected to rise to 375 million in 2050. Although there are many languages and dialects spoken in South Asia, it has many genetic, sociocultural, economic and nutritional factors common to its people. The common challenge that South Asian countries have to face is the leading cause of death of menopausal women, coronary heart disease (CHD).

Female Predisposition

Coronary heart disease is the leading cause of death among postmenopausal women worldwide and also in South Asia. Being a woman, whether in South Asia or elsewhere, carries certain risks for CHD. With natural estrogen providing a cardio protective effect, premenopausal women get CHD 10 years later than men but, when women get CHD, they fare worse than men. Post myocardial infarct (MI) mortality for women is higher than that for men for all ages and worse for younger women.¹

A greater proportion of women die before they are brought to hospital with sudden cardiac death (SCD). When

compared to men, more women with MI die of SCD before the arrival at a hospital.² This may be due to the older age and atypical symptoms in women. Further, over the years, the incidence of SCD in men has reduced whereas there is no such change in women. This is worse in South Asia where men get priority over women regarding care. This is apparent in findings of a study from Andhra Pradesh, where 79% of SCD in women were at home.³

Symptoms of CHD in women are somewhat different from typical male type of angina which are usually brought about by exertion and relieved by rest. In a large MI registry, a greater proportion of women than men presented without chest pain.⁴ Women with MI have atypical symptoms, like fatigue, shortness of breath and atypical chest pain. Exercise electrocardiogram (ECG) on treadmill is a test relied upon by cardiologists to diagnose the risk of CHD. Exercise ECG has lower sensitivity and specificity for women because of lower obstructive coronary artery diseases (CAD) prevalence.⁵ Coronary angiogram is the most important diagnostic tool, but women with CHD have more nonobstructive coronary artery disease as confirmed at autopsy. In the absence of a pathological block, in women there seem to be microvascular dysfunction possibly related to risk factor clustering and vascular inflammation.⁶ Coronary artery calcium (CAC) score as measured non-invasively provides an estimate of total atherosclerotic burden and therefore cardiac risk. Raggi et al studied about 10,000 asymptomatic men and women, referred for CAC screening and found that women were at higher risk of death at each level of calcification.⁷

Overall mortality is higher for women with MI, because of less obstructive disease and less aggressive management, commonly by thrombolysis, sedatives, reassurance. Even when procedures are used complications are higher. Percutaneous intervention (PCI) by balloon plasty or stents resulted in higher vascular complications and mortality for women.⁸ Risk adjusted mortality one year after coronary artery bypass grafting (CABG) for women has been 4.0% when compared with 3.2% for men.⁹

Prevalence

In the absence of reliable nationwide figures for prevalence, estimates of the burden of CHD on women in South Asia are based on cross-sectional surveys. In India, in the urban female of 45 to 54 years, the incidence of CHD was 10.5%

with an increase to 12.1% in the 55 to 64 years age group. The prevalence is nearly half in the rural setting.¹⁰ In a study in Pakistan, the prevalence has been 8.2% in women over 30 years,¹¹ whereas in Sri Lanka it is 12.99%.¹² In South Asia, there is a higher prevalence in women than in men, and a significant increasing trend in both urban and rural female population.

Mortality

South Asian women who migrated to other countries have a higher mortality rate from CHD than women of other ethnic origins.¹³ Women who are living in the South Asian region develop MI at a younger age than their counterparts in the rest of the world adding to the early CHD deaths, in their productive years. Seventeen percent of total female mortality is believed to be due to CHD in India. Projections from mortality figures in India show that over one million women would die of CHD in 2020.¹⁴

Risk Factors

Obesity, diabetes, hypertension, alcohol, tobacco use and dyslipidemia are the traditional risk factors, some of which are modifiable.

In the INTERHEART study when compared to other participants, South Asians have a stronger association of hypertension, high waist to hip ratio and adverse psychosocial factors with MI.¹⁵ The largest contributor to the population attributable risk for acute myocardial infarction in women in South Asian countries is high waist to hip ratio followed by lack of exercise, abnormal apolipoprotein B (Apo B), apolipoprotein A1 (Apo A1) ratio, lack of daily intake of fruits and vegetables and psychosocial factors.

Among the nontraditional and newer risk factors for CHD are high levels of lipoprotein(a) [Lp(a)], Apo B, triglycerides, and low-density lipoprotein (LDL), low levels of high-density lipoprotein (HDL) and elevated plasma homocysteine, plasminogen activator-inhibitor (PAI-1) and C-reactive protein (CRP).

Lipoprotein(a) has been shown to be an important determinant of CHD in both pre- and postmenopausal women. With the reduction of estrogen at menopause, there is an increase of Lp(a). Lipoprotein(a) molecule consist of an LDL particle, covalently bound to an apoprotein(a) molecule which has significant homology to plasminogen. Measurement of Lp(a) levels in cord blood in three ethnic groups in Singapore showed that Lp(a) of female newborns are higher than that of males, and Indian female newborns had the highest Lp(a) level, independent of birth weight and gestational age.¹⁶ This pattern continues in adulthood too as South Asian women had the highest level when compared to white women and men.¹⁷

Apolipoprotein B is present in very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), large-buoyant LDL and small dense LDL (SD-LDL), with one molecule of Apo B in each of these atherogenic particles. Thus, total Apo B reflects the total number of atherogenic particles. It is Apo B that leads to the entrapment of these lipoproteins in the arterial wall. Apo A1 is the major apolipoprotein in HDL particles and has a central role in the 'reverse cholesterol transport'. Apo B/Apo A1 ratio reflects the balance between the bad cholesterol particles and good cholesterol particles. In the INTERHEART study, Apo B/Apo A1 ratio has a strong relation with MI, and women have a higher ratio. Again South Asian women have a higher ratio than white women.

Very low density lipoprotein is associated with increased generation of small dense LDL particles which promote atherogenesis by rapid infiltration into the intima of arterial wall, increased susceptibility to retention in the extracellular matrix and increased oxidation and therefore is a strong risk factor for CHD. Very low density lipoprotein cholesterol of Asian-Indian women living abroad is much higher than that of male counterpart and white caucasian women.¹⁸

High density lipoprotein cholesterol has an inverse relationship with CHD. It is known to have anti-atherogenic properties by transport of excess cholesterol from arterial wall foam macrophages to liver and by its antioxidative action. High density lipoprotein concentration in plasma of South Asian women is significantly less than that of white Caucasian women.¹⁹

Hyperhomocysteinemia is an independent risk factor for CHD. It may be of interest to note, as vegetarianism is common in South Asia, low plasma B12 and folate levels contribute to high levels of homocysteine. South Asian women have a higher concentration of homocysteine when compared to women from the west and far east.²⁰

Plasminogen activator inhibitor-1 (PAI-1) contributes to inflammation, angiogenesis and atherogenesis. A rise of PAI-1 is associated with MI. In SHARE study (Study of Health Assessment and Risk in Ethnic groups), PAI-1 was higher in South Asian women when compared to Chinese and European women.²¹

Metabolic syndrome is a cluster of risk factors: obesity, increased blood sugar, increased triglycerides, reduced HDL and hypertension. Metabolic syndrome adds to the prediction of type 2 diabetes and CHD beyond that provided by individual components. Prevalence of metabolic syndrome in South Asia is higher than that of South East Asia and the Far East and is higher in women.^{22,23} In a national study in Sri Lanka, prevalence of metabolic syndrome in women was higher than that of men with a marked increase after menopause.²⁴

Obesity is considered to be a modifiable risk factor for CHD. South Asian women have high percentage of deep subcutaneous and visceral fat. South Asian newborns are of low birth weight, and intrauterine undernutrition leads to the 'thin-fat' baby, who is thin but has relatively high subcutaneous fat. Intrauterine adipogenesis with postnatal positive energy balance leads to adult adiposity, which is further aggravated in women at menopause by estrogen deficiency. Among adipokines secreted by adipocytes, leptin enhances insulin resistance and endothelial dysfunction, while adiponectin has the opposite effect. Females have higher insulin levels at birth than males.²⁵ South Asian newborns have higher levels of insulin than their white counterparts which increase continues to adulthood and menopausal age.

C-reactive protein plays a direct role in promoting inflammation which has a role in pathogenesis of atherosclerotic plaques. High sensitivity CRP (HS-CRP) levels are useful in CHD risk prediction,²⁶ and CRP in South Asian women is higher than that in women of Chinese or European origin.²⁷

Physical Activity

South Asian women participate in substantially low levels of physical activity when compared to women in other cultures due to social and cultural attitudes. In the INTERHEART study, lack of moderate to severe exercise is considered as a major risk factor for CHD in South Asian women.

Diet

Dietary saturated fatty acid is a principal determinant of total cholesterol and CHD and its consumption is highest in South Asia. Trans fats formed by partial hydrogenation of vegetable oils are commonly used in South Asia and results in higher TC/HDL ratio.²⁸ Although vegetarianism is common, high use of refined carbohydrates and trans fat containing ingredients as vanaspati, margarine, ghee, etc. and cooking habit of deep frying and reuse of oil, add to the atherogenic effect of food. Increased consumption of fruits and vegetables is associated with lowering of CHD incidence.²⁹ The INTERHEART study analysis shows lower prevalence of fruit and vegetable intake among South Asian women.

Urbanization

Urbanization, by changes in dietary patterns, reduced physical activity and psychosocial changes lead to an increase in the risk of CHD. Coronary heart disease prevalence in urban Indian population is higher than that in

rural setting.³⁰ In Sri Lanka, metabolic syndrome in urban women was significantly higher than that of rural women.²⁴ 28.33% of the population in South Asian countries live in urban areas and this is ever increasing with development as the annual growth of urbanization is about 3 to 6%.³¹

Prevention

Conventional risk factors do not explain the high prevalence and mortality among South Asian women. Gene polymorphisms and gene expression seem to contribute to this predisposition. As there is a dearth of studies on CHD in South Asian women of mid life, more research is needed on women living in the region. However in various preventive strategies, many modifiable factors need to be targeted. It is prudent to advocate community programs and policy changes at national level to promote healthy diet, reduce obesity and increase physical activity.

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