

# Childhood cardiovascular risk factors in South Asians: A cause of concern for adult cardiovascular disease epidemic

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## ABSTRACT

Cardiovascular risk factors in children are increasing at an alarming rate in the western world. However, there is limited information regarding these in the South Asian children. This review attempts at summarizing such evidence. South Asians are remarkable for the earlier onset of adult cardiovascular disease (CVD) by almost a decade compared to the Caucasians. We identified published literature, mainly on PubMed, Embase and Cochrane library using specific search terms such as lipid abnormalities, high blood pressure, hyperglycemia, tobacco use, obesity, physical inactivity, and unhealthy dietary practices. Atherosclerotic CVD processes begin early in childhood and are influenced over the life course by genetic and potentially modifiable risk factors and environmental exposure. 80% of adult CVD burden will fall on the developing nations by 2020. The concept of primordial prevention is fast emerging as a necessary prevention tool to curb adult CVD epidemic. Established guidelines and proven preventive strategies on cardiovascular health exist; however, are always implemented half-heartedly. Composite screening and prediction tools for adults can be adapted and validated in children tailored to South Asian population. South Asian children could be at a greater risk of developing cardiovascular risk factors at an earlier stage, thus, timely interventions are imperative.

**Keywords:** Cardiovascular disease, childhood, coronary heart disease, risk factors, South Asians

## INTRODUCTION

Coronary heart disease (CHD) manifests a decade earlier<sup>[1,2]</sup> with an increased prevalence in South Asians as compared to other ethnic groups, and the average age of stroke is much lower than in western countries.<sup>[3,4]</sup> Such a phenomenon can be attributed to atherosclerotic processes initiated early in childhood and being affected over the life course by both genetic and environmental interactions.<sup>[5,6]</sup> Such underlying pathogenesis underscores the significance of earlier cardiovascular risk factor screening in at risk children and youth, which can be tracked to predict future levels.<sup>[7-10]</sup> Nevertheless, the specifics of the transition from

these risk factors in childhood to overt cardiovascular disease (CVD) in adulthood are not clear.<sup>[9,11]</sup> Such gaps in knowledge base have prompted evidence based initiatives for high risk individuals and population centric approaches for primordial/primary prevention of CVD in children and youth. Such approaches may be more effective to prevent the development of risk factors rather than attempting to reverse the atherosclerotic risk in adulthood.<sup>[7]</sup> The aim of this review is to synthesize the clinico pathological and epidemiological evidence for clinicians of South Asia to promote preventive pediatric cardiovascular health.

We abstracted the most significant published literature on the electronic databases (all in English language), namely, Pub Med, Embase and Cochrane Library applying specific search terms such as “South Asians” “pediatric”; “childhood”; “CVD”; “CHD”; “physical inactivity”; “Diabetes mellitus”; “hypertension”; “dyslipidemia”; “smoking” etc. We have also gone through abstracts of conference/meetings; consulting authors/experts in the field; text books; publications of governmental/non-governmental organization.

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## EVIDENCE FOR CARDIOVASCULAR DISEASE RISK FACTORS IN CHILDHOOD

A consistent body of evidence from epidemiological, clinical and laboratory studies on cardiovascular risk factors among the younger populations, including children, adolescents, and youth exists worldwide.<sup>[8-10]</sup> However, such evidence is mainly confined to developed countries.<sup>[10]</sup> In India and the rest of South Asia, similar studies systematically evaluating cardiovascular risk factors across younger populations are generally inadequate. Such evidence synthesis is essential to help develop cost-effective screening and intervention programs in a specific population group.

### Clinico pathological and Imaging studies

Randomized controlled trials documenting the effect of risk reduction in childhood on the development of CVD in adults, are lacking.<sup>[12,13]</sup> However observations from Bogalusa,<sup>[14]</sup> pathobiological determinants of atherosclerosis in children and young adults (PDAY)<sup>[15,16]</sup> and Muscatine<sup>[17]</sup> studies provide compelling evidence linking potentially modifiable cardiovascular risk factors and CVD in adults, and thus support the need for preventive interventions early in life.<sup>[5,6]</sup>

### Epidemiological studies

Epidemiological studies from South Asia<sup>[10,18-20]</sup> provide reliable data regarding prevalence and trends of cardiovascular risk factors in children and youth. These studies have confirmed that the cardiovascular risk factors begin early, track through young age and tend to magnify and manifest in middle age in most societies.<sup>[21,22]</sup>

## INTRAUTERINE RISK FACTORS FOR ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

South Asia has high rates of poverty, gender inequalities, illiteracy, ignorance and religious beliefs towards pregnant mothers that contribute to fetal and early infant undernutrition with long-term negative health consequences.<sup>[21,23]</sup> Evidence from birth cohort studies have linked maternal glucose intolerance,<sup>[24]</sup> diabetes,<sup>[25]</sup> hypercholesterolemia,<sup>[26]</sup> vitamin D,<sup>[27]</sup> vitamin B12 status,<sup>[28]</sup> placental morphology<sup>[29]</sup> and birth weight<sup>[21,22]</sup> with childhood onset of adult disease. Therefore Barker's Thrifty phenotype hypothesis<sup>[30]</sup> and Neel's Thrifty Genotype hypothesis<sup>[31]</sup> are of particular relevance in South Asia.

## CARDIOVASCULAR RISK FACTORS IN CHILDREN

Most of the potentially modifiable risks factors that affect

children can be controlled early in life, lowering the risk of heart disease later in life.<sup>[7]</sup> They are enumerated below.

### Physical inactivity

Physical inactivity is a major modifiable risk factor for CVD.<sup>[32]</sup> The health benefits associated with physical activity include weight control, lower blood pressure, improved psychological well being and decreased risk of CVD.<sup>[33]</sup> However, unfortunately, physical activity levels in children are decreasing mainly from sedentary life-style entertainments. The recommended frequency of 150 minutes of physical activity for elementary schools and 225 minutes for middle/junior and senior high schools per week<sup>[34]</sup> including a mix of recreational and organized aerobic activities based on child's age, sex, race, sexual maturity, size, skill and social class should be implemented.

### Smoking

Tobacco smoking is an important and modifiable cardiovascular risk factor.<sup>[35]</sup> Both smoking and smokeless tobacco is equally prevalent amongst the youth of developing countries.<sup>[36]</sup> A recent Indian study reports more than 25% in 13- to 15-year-olds to be tobacco users, contributing to 17% of current total tobacco users.<sup>[37]</sup> More than 80% established adult smokers initiate smoking before the age of 18 years.<sup>[38-40]</sup> Hence, there is an urgent need to intervene early.<sup>[40]</sup> There are numerous interacting determinants that influence smoking behavior.<sup>[41]</sup> Environmental factors (sociocultural, economic and political) and personal characteristics like demographics, personality, education, and information are main influences in smoking initiation in children.<sup>[42]</sup> Prenatal maternal smoking has immediate and long-term adverse birth outcomes, including the onset of adult chronic diseases. Therefore, targeting smoking cessation among pregnant women should contribute to a healthy intergenerational effect.

### Obesity

Obesity in childhood and adolescence is attaining an epidemic proportion at about 15–20% in India.<sup>[43]</sup> Overweight and obesity in childhood are associated with diverse cardiovascular risk factors and has been shown to be related with premature atherosclerotic lesions.<sup>[33,44]</sup> Unlike in adults it is not possible to identify a single BMI (body-mass-index) cut off point as a threshold for defining obesity in children, as BMI changes with age across development.<sup>[45]</sup> Further, there is also a need for age and gender specific percentile based cut off points of anthropometric and metabolic variables in South Asian children and adolescents.<sup>[46]</sup> South Asia is facing the double burden of over and under-nutrition.<sup>[47-49]</sup> The South Asian newborns, children and adults have higher body fat compared to the Caucasians of similar body

weight, and cardiovascular risk manifests at a lower level of adiposity.<sup>[50]</sup> Obesity in South Asian children is also reported to be related with adverse lipid profile.<sup>[51]</sup>

### Insulin resistance and diabetes

Excess body fat, thick truncal subcutaneous fat, and abdominal adiposity are major predisposing factors for insulin resistance in South Asian children.<sup>[50]</sup> They manifest adiposity, insulin resistance and metabolic perturbations earlier in life with a higher magnitude than with children of other ethnic groups. Since the metabolic syndrome and obesity track into adulthood, these clinical entities need to be recognized early for effective prevention of diabetes and CVD.<sup>[7]</sup> Insulin resistance and hyperinsulinemia are early metabolic manifestations and should be incorporated to define insulin resistance and metabolic syndrome in these children.<sup>[46]</sup>

### Hypertension

Childhood hypertension is a recognized predisposing factor of adult hypertension as reported in the Bogalusa Heart Study.<sup>[52]</sup> Current guidelines suggest that children  $\geq 3$  years of age have to get their blood pressure measured during their routine health assessment.<sup>[53]</sup> Hypertension in children is defined as systolic or diastolic blood pressure steadily above 95<sup>th</sup> percentile on three different occasions.<sup>[33]</sup> Furthermore children have a 10% higher risk of developing hypertension in adulthood for each 1 to 2 mmHg increment of systolic BP.<sup>[54]</sup> These guidelines need to be validated and re-examined in South Asian children for population-specific reference values.<sup>[20,55]</sup>

### Dyslipidemia

Epidemiological studies have established positive relationship between conventional dyslipidemia in patients of CVD and their children.<sup>[56,57]</sup> Lipid abnormalities in children indeed contribute to adult CVD.<sup>[51]</sup> However, such traditional lipid risk factors do not explain fully the increased susceptibility of South Asians to CVD.<sup>[58]</sup> Hence, there is a strong need to identify the nontraditional lipid risk factors in childhood such as alterations in serum levels of Lp(a), Apo A-I, and Apo B-100 in children of premature South Asian CVD patients.<sup>[56,59]</sup> Consequently, emerging concepts like Lipid Tetrad Index [Total cholesterol x triglycerides x Lp(a)/HDL Cholesterol],<sup>[60]</sup> Lipid Pentad Index [Total Cholesterol x Triglyceride x Lp(a) x Apo B-100]/Apo A-I<sup>[59]</sup> and Atherogenic Index [Log(Triglycerides/HDL Cholesterol)]<sup>[61]</sup> are to be validated to explain the risk profile of premature CVD in South Asian children and youth. Cholesterol levels track over time,<sup>[33]</sup> and it is interesting to note that adult serum lipid and lipoprotein levels are observed in children as young as 2 years of age.<sup>[62]</sup> Consequently, the United States (US) national cholesterol education programme suggested at-risk children screening based on a family history of

premature CHD or parental dyslipidemia after 2 years of birth.<sup>[63]</sup> Nonetheless, gender and ethnic-specific guidelines of similar nature are important potential tools for certain pediatric populations.<sup>[64]</sup>

### Family history of cardiovascular disease

Family history of CVD encompasses genetically transmitted risk along with shared environment and behaviors influencing modifiable risk factors.<sup>[12]</sup> It is an important step in screening children's risk, as CVD tends to cluster in families and is a proxy for inherited tendency for coronary risk. It is an independent CHD risk predictor.<sup>[8]</sup> Family history of premature CHD is defined as a documented myocardial infarction, angiographic documentation of CHD, angina pectoris, or sudden cardiac death in first or second degree relatives (parents, siblings, grandparents, or blood-related aunts and uncles)  $\leq 55$  years of age.<sup>[33]</sup> However there is paucity of data regarding this from South Asia.

### Ethnicity

Disproportionate predilection of CVD in South Asians<sup>[4,65]</sup> is due to genetic predisposition mediated by high lipoprotein (a)<sup>[66,67]</sup> and cardiovascular risk factors potentiated by environment or life style.<sup>[4]</sup> South Asians are genetically susceptible to CVD from early childhood.<sup>[7]</sup> Ethnic differences in lipids, lipoproteins, insulin resistance and blood pressure are well documented in adults and begin early in childhood.<sup>[68,69]</sup> South Asian children demonstrate increased levels of insulin and insulin resistance in contrast to Caucasian children.<sup>[69,70]</sup> Such ethnic differences in insulin resistance are not correlated with matching differences in adiposity. However, insulin metabolism seems to be more sensitive to a known degree of adiposity among South Asian children.<sup>[69]</sup>

## CONCLUSIONS

In conclusion, available evidence regarding the conventional risk factors for cardiovascular disease in south Asian children is reviewed. This review underscores the need for more data collection. The situation of cardiovascular risk factors in children is concerning. Risk factor modifications earlier in childhood may control the burgeoning epidemic of adult CVD in south Asia.

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