Body Composition and the Metabolic Syndrome in Asian Indians: A saga of multiple adversities

Asian Indians have been shown to have high prevalence rates of the metabolic syndrome (clustering of abdominal obesity, hypertriglyceridaemia, low levels of high density lipoprotein cholesterol, glucose intolerance and procoagulant tendency), diabetes mellitus and coronary heart disease (CHD).\(^1\)\(^-\)\(^3\) Most of the information on this metabolically disadvantaged ethnic group is based on studies on migrant Indians.\(^1\) However, the incidence and prevalence rates of diabetes mellitus,\(^2\) cardiovascular risk factors and CHD\(^4\)\(^-\)\(^5\) are rising in India as well. Despite global attention and several investigations, the cause(s) remains speculative.

Obesity is a forerunner of the metabolic syndrome and contributes significantly to atherosclerotic vascular disease. Interestingly, applying the World Health Organization (WHO) criterion [body mass index (BMI) >30 kg/m\(^2\)], many studies have shown a <10% prevalence of obesity in India,\(^6\)\(^,\)\(^7\) although much higher figures have been reported in immigrant Indians.\(^1\) The evidence suggests that the body composition abnormalities of Asian Indians may have an important bearing on the pathogenesis of metabolic derangements. First, their body fat is more and muscle mass lesser as compared to other Asian ethnic groups, Caucasians and African–Americans.\(^8\)\(^-\)\(^10\) Indeed, some Indians considered ‘non-obese’ by the WHO criteria of BMI cut-offs are actually obese when body fat is used to define obesity.\(^8\) Second, and perhaps equally important, is the high prevalence of abdominal adiposity even in people who are otherwise considered non-obese.\(^11\)\(^,\)\(^12\) While some investigators have stressed that Asian Indians have a higher intra-abdominal fat mass,\(^10\) others have reported an excess of truncal subcutaneous fat\(^13\) as compared to Caucasians. It is uncertain whether the subcutaneous abdominal or intra-abdominal adipose tissue is more important for the pathogenesis of insulin resistance.\(^14\)\(^,\)\(^15\) However, Asian Indians probably have an excess of adipose tissue at both the sites. Further, Indian women have many such features that become accentuated post-menopause. It is well known that any such abnormality of body composition may decrease insulin-mediated glucose uptake in the skeletal muscle and adipose tissue, and induce insulin resistance that may well initiate glucose intolerance and dyslipidaemia. What is disturbing is that this type of body composition has been reported even at birth\(^16\) and the metabolic disturbances have been shown to manifest during early childhood\(^17\) in Asian Indians. These observations have important implications. First, the excess metabolic and cardiovascular risk of Asian Indians may be partly accounted for by the excess body fat and abdominal adiposity. Second, the internationally accepted definition of normal range of BMI, and those for defining generalized obesity (by BMI) and abdominal obesity (by waist circumference), which are mostly based on the data of Caucasian populations, may not be applicable to Asian Indians as well as other Asian ethnic groups.\(^18\) For a general physician, it may mean advising therapeutic lifestyle measures (diet and exercise) for Asian Indian patients at a lower level of BMI than is presently recommended. For an individual, it would mean maintaining the body weight rigorously within the optimal range. However, the implication of these observations for the drug therapy of metabolic disorders (e.g. use of metformin for obese type 2 diabetic patients) is not clear. There is a suggestion that a lower cut-off of BMI should be considered for initiating therapy for such patients.\(^19\) It is believed that lowering the BMI cut-off by about 3 units would increase the prevalence of obesity in a population by about 10%–15%, thus increasing the burden on national health resources.\(^20\)

Most investigators have researched excess body fat or regional accumulation of adipose tissue in Asian Indians. Perhaps equally important, for the insulin–glucose
metabolism in subjects with such a body phenotype, but not investigated, are the potential consequences of an altered ratio of body fat and fat-free mass, and alterations in lean tissues. While the skeletal muscle mass is less in Asian Indians it is not known whether it is physiologically altered. Further, whether liver metabolism is also altered in this population has not been investigated. These issues are important since skeletal muscle and liver tissues are critical to the glucose–insulin–lipid metabolism in humans.

If the characteristic phenotype of Asian Indians occurs as early in life as birth, then, logically, the possible aetiological factors are present before this event. It is reasonable to expect that genetic traits may be responsible for such predisposition, and could influence body composition, as well as the development of diabetes and CHD singly or in combination. In other ethnic groups it has been shown that genetic factors could influence birth weight, body composition and body fat patterning. It is also possible that Asian Indians have a higher magnitude of insulin resistance independent of generalized and regional adiposity, arising de novo or genetically directed as reported for hepatic insulin resistance.

The other possible contributory factors to the altered body composition and insulin resistance and relevant for a developing country such as India, is in utero or early-life adverse events, primarily poor nutrition. It has been shown that those with a low birth weight may have increased prevalence rates of hypertension, diabetes, CHD and insulin resistance later in life, particularly when these subjects gain excess adiposity in early childhood. It has been speculated that as a measure of adaptation the storage of body fat is accelerated and lean tissues suffer from attrition due to protein malnutrition. Adverse factors may affect other tissues as well such as pancreatic β-cells, vascular endothelium and renal tubules, which may lead to decreased insulin secretion, endothelial dysfunction and microalbuminuria, respectively. The hypothesis is attractive but remains to be critically tested. Moreover, there seems to be a modulation of the adverse milieu in utero or during early life by the genomic profile of the individual that may reset the foetal programming. Later in life, diet or other unknown environmental influences may operate as ‘amplifiers’ for this phenotype. Although not necessarily related to adverse early-life events, Asian Indians have significant endothelial dysfunction, which may adversely affect proinflammatory cytokines (interleukin-6 and tumour necrosis factor-α), nitrous oxide, endothelin-1, expression of cell adhesion molecules and procoagulant activity. All these derangements could initiate and exacerbate insulin resistance and accelerate atherosclerosis. Also, the subclinical inflammation that may be a consequence of dysregulated proinflammatory cytokines has been reported to be more prevalent in Asian Indians than in the Caucasian population. Importantly, there is a strong suggestion from recent studies that subclinical inflammation predicts the future development of diabetes and risk of CHD.

Recent research has also shown metabolic dysregulation related to the accumulation of fat in body tissues where it is usually not present. First, excess fat accumulation in the skeletal muscle (intramyocellular triglycerides, IMCL), non-invasively measured with proton magnetic resonance spectroscopy, has been correlated with insulin resistance. Interestingly, IMCL accumulation in the soleus muscle, although reported to be high in South Asians in the UK, and in non-obese subjects with excess body fat in India, was not associated with insulin resistance, unlike that shown for Caucasians. Second, accumulation of fat in the liver (hepatic steatosis) not induced by alcohol intake and usually occurring in obesity and diabetes mellitus, has been shown to be associated with insulin resistance. It is also known to be present in lipodystrophies, which are associated with severe insulin resistance in patients with a lack/loss of body fat. Hepatic steatosis, previously believed to be a benign disorder, may lead to steatohepatitis and infrequently cirrhosis. It is not unreasonable to speculate that in the presence of excess body fat and insulin resistance, as is the case with Asian Indians, the prevalence of hepatic steatosis may be high. However, no data are currently available.

Whatever the contributions of the genetic or constitutive traits in the development of body composition and the metabolic syndrome in Asian Indians, environmental and
lifestyle factors have an important and sometimes overriding influence. Attributes of two migrant Indian population subgroups clearly illustrate this argument. First, rural-based populations in India have a low prevalence (nearly half or less compared to urban ones) of obesity, hypertension, diabetes, dyslipidaemia and CHD. One of the important reasons could be that these people have a physically vigorous lifestyle and consume low-calorie, low-saturated fat diets. When people living in rural areas migrate to metropolitan cities and settle in urban slums, they tend to become obese, glucose intolerant and dyslipidaemic, as a result of changes in their activity pattern and dietary profile. Second, Asian Indians settled in other countries, who are generally affluent, have a higher mean BMI, abdominal adiposity and serum cholesterol levels compared to Indians in India. Although there are few studies that have directly compared such migrant and non-migrant Indian populations, it appears that increasing urbanization, mechanization and imbalanced diets may be responsible for the transition to unfavourable body composition and metabolic profile. Recent trends in India show a substantial migration of people from rural to urban areas and rapid and widespread adaptation of a ‘western’ diet and lifestyles that may be important contributors to the ‘diabetes and CHD epidemic’. The role of Indian diets in causing obesity and dyslipidaemia continues to be controversial. Indeed, a more consistent adverse lifestyle factor of Asian Indians is physical inactivity. This is also responsible for the apparent delineation of rural and urban differences in body composition and cardiovascular risk. There is a consensus that regular physical activity can prevent the development of diabetes mellitus and could also decrease the risk of CHD. Specifically, recent preliminary studies show increasing obesity and an adverse anthropometric profile in children, adolescents and young adults in India who are also becoming more sedentary. Such individuals are at increased risk for early onset of diabetes, dyslipidaemia and accelerated atherosclerosis. It is unfortunate that for Asian Indians, who are weighed down by several inherent and acquired factors that enhance metabolic perturbations and cardiovascular risk, such simple preventive advice as increasing physical activity and limiting caloric and fat consumption have not percolated to the general population.

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