Body fat, metabolic syndrome and hyperglycemia in South Asians

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ABSTRACT

The prevalence of overweight and obesity is escalating in South Asian countries. South Asians display higher total and abdominal obesity at a lower BMI when compared to Whites. Consequently, metabolic dysfunction leading to metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM) will account for a majority of the health burden of these countries. In this review, we discuss those factors that contribute to MetS and T2DM in South Asians when compared to whites, focusing on adiposity. Abdominal obesity is the single-most important risk factor for MetS and its predisposition to T2DM. Excessive ectopic fat deposition in the liver (non-alcoholic fatty liver disease) has been linked to insulin resistance in Asian Indians, while the effects of ectopic fat accumulation in pancreas and skeletal muscle need more investigation. South Asians also have lower skeletal muscle mass than Whites, and this may contribute to their higher risk T2DM. Lifestyle factors contributing to MetS and T2DM in South Asians include inadequate physical activity and high intakes of refined carbohydrates and saturated fats. These are reflective of the recent but rapid economic transition and urbanization of the South Asian region. There is need to further the research into genetic determinants of dysmetabolism as well as gene x environment interactions. Collectively, MetS and T2DM have multi-factorial antecedents in South Asians and efforts to combat it through low-cost and socio-culturally appropriate lifestyle interventions need to be supported.

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1. Introduction

Metabolic syndrome (MetS) is a clustering of inter-related risk factors for type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). With the increasing global burden of obesity, there is continued interest in defining and examining the extent of MetS in population groups and whether its association with future T2DM and CVD is consistent or amplified across the ethnic composition of a population. MetS is generally diagnosed from the presence of at least 3 of the following 5 criteria; increased waist circumference (WC), hypertriglyceridemia, hypertension, hyperglycemia and low HDL cholesterol (HDL-c). Atherogenic dyslipidemia (high serum triglycerides and low levels of HDL-c) is a part of MetS, but it is particularly prevalent in South Asians.

While clustering of these metabolic derangements contributes to the mechanisms underlying MetS, abdominal adiposity is arguably the single most important criterion, as it is causally associated with the other four MetS criteria. Of note, WC is a simple and reliable anthropometric measure used in epidemiological studies as a surrogate for central adiposity. However, WC captures an estimate of the subcutaneous abdominal adipose tissue as well as the intra-abdominal adipose tissue. These two compartments are metabolically active and contribute significantly to metabolic derangements including insulin resistance and T2DM. Sex and race-ethnic differences in the relationship between WC and T2DM risk are well recognized, and account for the different WC cut-off points to determine risk of different ethnic groups. 1–4

The objective of this review is to discuss body fat and its distribution in South Asians in the context of MetS and T2DM. South Asians are ethnic groups assigned to natives and diaspora of India, Pakistan, Sri Lanka, Bangladesh, Nepal, Bhutan and Maldives, though the available literature mostly discusses the first four nations. In addition, there are substantial numbers of the South Asian diaspora settled in the US, UK, Europe, Asia (especially Malaysia and Singapore), South Africa, Mauritius and Fiji. Reference to these immigrant groups is only made when research data on South Asians living at native countries were unavailable.

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We have approached our objective through a consideration of potential lifestyle, environmental, genetic/epigenetic and fetal/developmental origins of the problem and present a schematic that underpins this review. Despite our primary focus on body fat, MetS, and T2DM in South Asians, a brief summary of the global standing of these issues is provided at the beginning of each section, to set the stage. We also identify the gaps in our present knowledge which could serve to drive future research agendas.

2. Search methodology

A literature search was conducted for studies on abdominal obesity and mechanisms for insulin resistance and T2DM from 1966 to March 2018 in the medical search database of PubMed (National Library of Medicine, Bethesda, Maryland, USA) and Google Scholar. Search terms were; “obesity”, “abdominal obesity”, “adiposity”, “ectopic fat”, “diet”, “metabolic syndrome”, “type 2 diabetes”, and “cardiovascular disease” in global and the South Asian/Asian Indian context. References from selected papers were also searched for other potential papers of interest. Data have also been accessed from publicly available sources such as the Global Burden of Disease (http://www.healthdata.org/), and the World Health Organization (http://who.int/en/).

3. Metabolic syndrome and obesity

The rising pandemic of obesity has led to an increase in the prevalence of metabolic syndrome (MetS). The economic transition occurring in developing nations has seen rapid changes in lifestyle and the living environment such that the increased burden of MetS and T2DM has been most acutely felt in Asia and Africa. We, however, acknowledge that the use of different criteria to define MetS, makes comparisons of MetS burden across nations rather difficult. We expand on this facet later since it has implications for public health policy and action.

The prevalence of overweight and obesity among adults in South Asian countries has increased over the past 25 years. Several studies show higher body fat, excess metabolic perturbations and cardiovascular risk factors at lower value of BMI in South Asians vs. White populations. The observations by Deurenberg-Yap et al. of high body fat in Asian Indians in Singapore at low level of BMI values has been supported by studies on Asian Indians residing in India and immigrant Asian Indians in USA. Several cardiovascular risk factors are imbalanced (high total cholesterol, low-density lipoprotein–cholesterol, and triglycerides and significantly lower HDL) in South Asians than whites at similar level of BMI and WC. Rajak et al. showed that for a given level of BMI, South Asians in Canada have elevated levels of blood glucose and lipid related factors were more likely to be present, and that cut-offs of BMI based on these factors were 6 kg/m2 lower as compared than in whites. In a cross-sectional study on 4672 Whites and 1348 migrant South Asian participants from ADDITION-Leicester (UK) cohort and 985 indigenous South Asians from North India, lower cut-points for obesity were derived for South Asians using fractional polynomial models with fasting and 2-hour blood glucose as outcomes, and ethnicity, objectively-measured BMI/waist circumference, their interactions and age as covariates. In a comparative study, the prevalence of diabetes was higher in studies in Indians residing in India as compared to Japan, China, and the rest of Europe. Further, the association between BMI and diabetes, adjusted for age, showed an increase in prevalence starting at a BMI between 15 and 20 kg/m2 in Indian populations compared to 25 kg/m2 in Europeans. Similarly, waist circumference cut-offs for south Asians are lower (≤80 cm in women and ≤90 cm in men) based on data from India and other countries.

In 2000 CE the World Health Organization (WHO) Expert Group, suggested redefining the criteria for obesity for people residing in Asia Pacific region; the proposed BMI criterion for overweight was 23–24.9 kg/m2 and that for obesity was ≥25 kg/m2. These and other data prompted the Indian Consensus Group in 2009 to define BMI levels of 23–24.9 kg/m2 for overweight and ≥25 kg/m2 for obesity. In 2013, a review of recent studies conducted on Asian-Americans by Hsu et al. showed occurrence of T2DM in Asian-Americans at a relatively lower BMI cut point. These authors emphasized that for screening for T2DM, a BMI cut-point of 23 kg/m2 is appropriate for Asian populations residing in USA, and the same has been stated in position statement for 2015 by American Diabetes Association. Importantly, lower BMI cut-points for metabolic surgery for obesity for Asian Americans vs. other ethnicities (27.5 vs. 30 kg/m2, respectively) have recently been emphasized.

The increasing prevalence of overweight since the year 2000 in several South Asian countries suggests that the prevalence of MetS will continue to rise in this region over the next decade, with consequent impact of prevalence of T2DM. This rise is substantially influenced by urbanization, mechanization and rural-to-urban migration. Most studies in South Asians report higher prevalence of MetS and T2DM in urban areas compared to rural areas. This is likely due to an effect of decreased physical activity combined with unhealthy diets leading to obesity; while the effect of less studied factors like increased pollution cannot be excluded.

Recent reports have estimated the prevalence of MetS in South Asia to be 26%, as per National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) definition. However, the estimated prevalence varies by the MetS definition, with higher prevalence estimated with NCEP, ATP III and modified NCEP, ATP III criteria than with the WHO definition. Among South Asian countries, the highest prevalence is seen in Pakistan (by NCEP, ATP III definition: 31.0%) while lowest prevalence is seen in Nepal (by NCEP, ATP III definition: 20.7%).22,23 According to NCEP, ATP III definition, MetS prevalence among rural Indian females (18.4%) was much lower than that among urban females (43.2%), while there was no difference observed among males (rural: 26.9%, urban: 27.7%).22,23 This suggests that India has a heterogeneous population with different groups at different stages of the epidemiologic transition, and any overall estimate may not be tenable unless there is a universal adoption of one classification system. In migrant South Asians, the prevalence of MetS was high too; 27% (31% men vs. 17% women): 59% had high WC (58% men vs. 62% women), and 47% had low HDL-C (46% men vs. 48% women).22,23 Indeed, among Asian population in USA, South Asians were more likely to have T2DM (adjusted OR: 4.88; 95% CI: 1.52–15.66) and MetS (adjusted OR: 5.59; 95% CI: 1.69–18.50) compared to Whites.22,23

There is also an ongoing debate about the utility of diagnosing MetS for the prediction of future T2DM and CVD, over the value of its individual components. For example, every increase in the number of MetS components, inflates the risk of both CVD and T2DM. However, some authors have shown that blood glucose level24 or glucose tolerance25 are better predictors of risk of T2DM than diagnosis of MetS.

4. Relationships between body fat, ectopic fat and dysmetabolism (Table 1)

Abdominal obesity is a pivotal risk factor for MetS, T2DM, atherosclerosis and CVD among all race/ethnic groups. In a large study spanning over 63 countries, the prevalence of abdominal obesity was specifically higher in South Asian as compared to White Caucasian and other ethnic groups. In Asian Indians, a higher prevalence of abdominal obesity is noted even at low levels of BMI. Obesity in south Asians is featured by high body fat percentage, increased total abdominal fat, intra-abdominal visceral fat, and truncal fat, in comparison to white Caucasians. Detailed comparison of body fat, body fat depots and adipocytes in South Asians in comparison to Whites and other ethnicities and their relevance to metabolic perturbations are provided in Table 1.

Further, even non-obese Asian Indians with T2DM have significantly higher volumes of total abdominal fat (19.4%), total intra-abdominal fat (49.7%), intra-peritoneal fat (47.7%), and retroperitoneal fat (70.7%).
have high glucagon levels and have high surrogate markers of insulin resistance (Anoop S, Misra A, unpublished, 2018) as compared to non-diabetic controls. Metabolically these are associated with lower glucose disposal rate and higher insulin resistance when compared to White Caucasians of similar BMI.

Irrespective of obesity, larger abdominal adipocyte size predicts insulin resistance as well as T2DM independent of insulin resistance. As compared to White Caucasians, South Asians have larger adipocytes correlating with significant insulin resistance in non-diabetic men. Further, adipocyte areas were higher in Asian Indians who had increased body fat percentage and hepatic fat as compared to White Caucasians. Adipocyte hypertrophy leads to its asphyxia and dysfunctional metabolism and decreased triglyceride storage which in turn, leads to overflow of fatty acids to intra-abdominal visceral fat and liver and low adiponectin levels. It is also noteworthy that subcutaneous abdominal adipose tissue mRNA expression was significantly higher for genes associated with inflammation, CD68, MAC1 (Macrophage-1 antigen), and MCP1 (Monocyte Chemoattractant Protein-1) in Asian Indians compared with whites. Overall, available data, though restricted to a few studies, suggest that a heightened inflammatory state is present in subcutaneous adipocytes of South Asians.

5. Ectopic fat

Comparative data of ectopic fat depots and metabolic relevance between South Asians and whites has been researched by various groups worldwide and are summarized in Table 1. Only some important issues are discussed in detail below.

5.1. Liver

Relationship of insulin resistance and MetS with ectopic adipose tissue depots continues to be investigated. Deposition of triglycerides in the liver (non-alcoholic fatty liver disease, NAFLD) is an important component of MetS as it could potentially disrupt glucose–insulin metabolism. A causal relationship between NAFLD and hepatic insulin resistance, MetS and CVD has been demonstrated in non-diabetic and diabetic individuals. Using phosphorous magnetic resonance spectroscopy (MRS), significant derangements of hepatic gluconeogenesis pathway was shown in normo-glycemic, normo-lipidemic and normo-tensive Asian Indians with NAFLD. Importantly, in the only comparative study to date, accumulation of liver fat was >2 folds higher in non-obese, non-diabetic Asian Indians vs. Whites living in USA, and showed stronger associations with the insulin resistance in former. Overall, it appears that NAFLD is strongly related to metabolic dysfunction and cardiovascular risk factors in Asian Indians.

5.2. Pancreas

Fat accumulation in pancreas, i.e. non-alcoholic fatty pancreas disease (NAFPD) is relatively less investigated vis-à-vis insulin resistance and MetS and T2DM. A preliminary communication has reported a cut-off of 6.2% to define excess pancreatic fat. Such fat accumulation may result in pancreatic inflammation and fibrosis (similar to that of NAFLD), and loss of β-cell mass and function, which may lead to hyperglycemia. Such a scenario of β-cell failure as a result of fewer β-cells at birth, exposure to apoptotic triggers such as fat in the pancreas, and high demand from insulin resistance, has been hypothesized to result

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**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Difference relative to White Caucasians/other ethnicities</th>
<th>Comment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body fat</td>
<td>Increased</td>
<td>Relevance of excess total body fat alone to insulin resistance is not clear</td>
<td>Deurenberg-Yap et al.6, Gao et al.28, Anand et al.28b, Lear et al.39c</td>
</tr>
<tr>
<td>Truncal and abdominal subcutaneous fat</td>
<td>Increased</td>
<td>Related to insulin sensitivity and metabolic syndrome, diabetes.</td>
<td>Petersen et al.43b, Garg et al.42d</td>
</tr>
<tr>
<td>Intra-abdominal visceral fat</td>
<td>Increased</td>
<td>Related to decreased glucose disposal rates and dyslipidemia. Gender differences.</td>
<td>Bakker et al.44b, Admiraal et al.45b</td>
</tr>
<tr>
<td>Thigh subcutaneous adipose tissue and skeletal muscle lipids (intra-myocellular triglycerides)</td>
<td>Increased</td>
<td>Thigh subcutaneous tissue protective for diabetes</td>
<td>Eastwood et al.37c, Forouhi et al.38b, Sinha et al.39l</td>
</tr>
<tr>
<td>Hepatic fat (non-alcoholic fatty liver disease)</td>
<td>Increased</td>
<td>Related to increased insulin resistance and pro-inflammatory cytokines. Association with CVD.</td>
<td>Petersen et al.43b, Garg et al.42d</td>
</tr>
<tr>
<td>Epicardial fat</td>
<td>No comparative data. Increased pancreatic volume (surrogate of excess fat) shown in Asian Indians</td>
<td>Research needed if related to insulin secretion and insulin resistance</td>
<td>Misra et al.39f</td>
</tr>
<tr>
<td>Pancreatic fat (non-alcoholic fatty pancreas disease)</td>
<td>Lesser BAT volume</td>
<td>Conflicting data on BAT activity Lower related to less resting energy expenditure</td>
<td>Bakker et al.44b, Admiraal et al.45b</td>
</tr>
<tr>
<td>Brown adipose tissue (BAT)</td>
<td>Increased</td>
<td>Conflicting data</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous adipocytes</td>
<td>Increased</td>
<td>Increased insulin resistance and MetS and T2DM. A preliminary communication has reported a cut-off of 6.2% to define excess pancreatic fat</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Gulati and Misra and other reviews. Although most studies compared Asian Indians/South Asians with whites/White Europeans, others have included individuals from other ethnic groups also. Deurenberg-Yap et al.6 have compared Chinese, Malays, and Indians; Marinou et al.35 compared Europeans, South Asians and Afro-Caribbeans; Petersen et al.40 compared Eastern Asians, Asian-Indians, Blacks, Caucasians, and Hispanics; and Garg et al.41 compared Asian Indians with whites, blacks, Latinos, and Chinese Americans.

a Adjusted/matched for BMI.
b Adjusted for age, income, smoking status, and BMI.
c Adjusted for BMI, body fat and age.
d Adjusted for age, income, smoking status, and BMI.
e Adjusted for BMI and age.
f Adjusted for total fat.
g Adjusted/matched for age, sex, BMI.
h Matched for age and BMI.
i Adjusted for total fat.
j Adjusted for BMI and known risk factors.

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- Adjusted/matched for BMI.
- Adjusted for age, income, smoking status, and BMI.
- Matched for BMI, body fat and age.
- Adjusted for age, income, smoking status, and BMI.
- Adjusted for BMI and age.
- Adjusted for total fat.
- Adjusted/matched for age, sex, BMI.
- Matched for age and BMI.
- Adjusted for total fat.
- Adjusted for BMI and known risk factors.
in T2DM in South Asians, although there is paucity of research data. In an MRI-based case–control study on non-obese (BMI < 25 kg/m²) Asian Indians with T2DM, higher pancreatic volume (26.6%) and pancreatic volume index (21.3%) were reported in cases as compared to controls. In this study pancreatic volume correlated significantly with multiple measures of abdominal obesity and liver span.

5.3. Skeletal muscle

Another depot of ectopic fat is skeletal muscle i.e. intra-myocellular lipids (IMCL). These minute lipid droplets are distributed throughout the muscle cytoplasm and constitute an important form of energy during physical activity. However excessive accumulation has been implicated in the pathogenesis of insulin resistance. The exact pathophysiological relationship between IMCL and insulin resistance is unknown despite intense interest in this field of research. The association of IMCL with insulin resistance in Asian Indians is sparsely researched. Using Proton magnetic resonance spectroscopy (MRS), higher IMCL content was found in non-obese Asian Indians with T2DM as compared to non-diabetic participants, correlating with waist circumference and waist hip ratio. Further, while South Asians in UK had higher body fat and lower insulin sensitivity than whites, IMCL was not associated with insulin sensitivity among South Asian men. The authors stated that mechanisms other that mediated through IMCL is responsible for insulin resistance in South Asians. Clearly, more research is needed on the links between ectopic fat deposition and skeletal muscle mass and dynamic measures of insulin sensitivity.

6. Low skeletal muscle mass, MetS and type 2 diabetes

While relationship of adiposity with MetS continues to be intensely examined, the relationship of MetS with skeletal muscle mass has not received similar scrutiny. As age advances, there is a reduction in muscle mass, muscle force and its repair capacity. Among women, the ability of muscle to generate force declines sharply following menopause, which is linked to decline in estrogen levels, leading to increased intra-myocellular triglycerides (IMTG). These minute lipid droplets are distributed throughout the muscle cytoplasm and constitute an important form of energy during physical activity. However excessive accumulation has been implicated in the pathogenesis of insulin resistance. The exact pathophysiological relationship between IMCL and insulin resistance is unknown despite intense interest in this field of research. The association of IMCL with insulin resistance in Asian Indians is sparsely researched. Using Proton magnetic resonance spectroscopy (MRS), higher IMCL content was found in non-obese Asian Indians with T2DM as compared to non-diabetic participants, correlating with waist circumference and waist hip ratio. Further, while South Asians in UK had higher body fat and lower insulin sensitivity than whites, IMCL was not associated with insulin sensitivity among South Asian men. The authors stated that mechanisms other that mediated through IMCL is responsible for insulin resistance in South Asians. Clearly, more research is needed on the links between ectopic fat deposition and skeletal muscle mass and dynamic measures of insulin sensitivity.

7. Early loss of beta cell function

While increased insulin resistance among South Asians has been recognized, studies suggest that early loss of beta cell function could be yet another factor which predisposes South Asians to T2DM. It has been shown that beta cell function declines rapidly even at the stage of pre-diabetes, especially in those who have combined impaired glucose tolerance and impaired fasting glucose. Recent data show decreased beta cell function in Asian Indians even at the stage of ‘normal glucose tolerance’, specifically in those who have only elevation of the 1-hour glucose value during oral glucose tolerance test. While the exact causes of the early loss of beta cell function is not known, it could be due to combination of genetic/environmental factors and is probably related to high carbohydrate diet/physical inactivity (see discussion regarding these factors below).

8. Cortisol and adipocytokines

Several adipocytokines have been studied to understand the increased propensity for MetS, most prominently, adiponectin and leptin. Adiponectin increases with age and is generally higher among women than men, but lower among obese and those with T2DM. Similarly, leptin plays a causal role in diet-induced obesity. South Asians have lower circulating adiponectin, higher resistin and higher leptin levels compared to Europeans. Additionally, the relationship of adiponectin and insulin resistance varies by race/ethnic group, such that a unit decrease in adiponectin is associated with a greater increase in insulin resistance among South Asians relative to Europeans, confirmed recently in a study from Singapore. Also, relative to other ethnic groups, even lean, young South Asian men have higher insulin resistance, and also higher interleukin-6 levels even after accounting for insulin resistance. Of importance, total adiponectin concentration progressively decreased across the glucose spectrum in Asian Indians, associated with insulin resistance. It was postulated that the South Asian diaspora have an adverse adipocytokine profile which deteriorates further with glucose dysregulation.

The role of hypothalamic-pituitary axis (HPA) and cortisol in pathophysiology of obesity and related disorders continues to be debated. Indeed, pathological HPA axis activity has been shown to be significantly related to anthropometric, metabolic and hemodynamic markers of cardio-metabolic disease. There is an increasing interest whether greater serum cortisol may account for the association of stress and the MetS. Clinically significant cortisol excess (as seen with Cushing’s Syndrome) has many features of the MetS, and hence a role for cortisol could include increased food intake, reduced insulin sensitivity, stimulation of adipogenesis, differential regulation of lipoprotein lipase, and fat accumulation in liver and muscle. While one study reported significantly lower cortisol in South Asians relative to Europeans the links between cortisol and components of MetS were much stronger in South Asians compared to Europeans, irrespective of between-group differences in cortisol.

9. Metabolic syndrome and CVD in South Asians

Presence of MetS is well accepted as a risk factor for CVD and CVD-related mortality. The South Asian ancestry may contribute the greatest proportion to the global burden of CVD. It was important to investigate whether MetS played a similar or greater role in development of CVD in South Asians. In a large cross-sectional survey in India, there was an increased risk of ‘probable’ coronary artery disease (CAD) with increasing MetS, though the proportion of persons with ‘possible’ and ‘probable’ CAD varied with classification system used and gender. [WHO > International Diabetes Federation (IDF) > National Cholesterol Education Program, Adult Treatment Panel (NCEP, ATP III) [in men, but not women]. This gender bias in detection was possibly due to inclusion of insulin resistance in WHO criteria, and insulin resistance associates
better with metabolic abnormalities in men than in women.70 In one comparative study of South Asians and whites, Tillin et al.5 observed that the odds ratio (OR) for developing CAD in South Asians with MetS vs. their white counterparts varied with the MetS classification, being higher in South Asians with the NCEP ATP III criterion but similar with WHO criterion. Overall, South Asians have high prevalence of MetS, but the limited data are available regarding their progression from MetS to CVD.

10. What is it about South Asians that may confer this added cardiometabolic risk?

There may be a combination of factors responsible for enhanced risk for MetS and T2DM in South Asians and the most researched factors are discussed in the following sections.

11. Nutrition

Rapid strides in urbanization, globalization, growth of economy, emerging new technologies and evolving agricultural practices have led to increased availability, accessibility and affordability of more packaged and processed foods such as refined grains, added sugars, edible refined oils and fats in South Asia.46 This has resulted in rapid nutrition transition occurring in South Asian countries, leading to an escalation in obesity-related MetS and T2DM both among adults and children.17 Several dietary imbalances have been reported in South Asian countries. Most importantly, nearly 60–75% of daily calories come from refined carbohydrate foods with high dietary glycemic load (derived mainly from highly polished white rice or wheat) in both urban and rural settings of India.71–73

The following sections summarize the key issues in nutrition in Asian Indians/South Asians which may be related to insulin resistance, MetS, and T2DM.

11.1. Carbohydrates

In Asian Indians, refined grain consumption shows a strong association with insulin resistance, high serum triglyceride levels, and increased waist circumference.74 Further, dietary carbohydrates, and specifically, the dietary glycemic load, were also associated with risk for T2DM among urban Indians.74 High intake of refined carbohydrates and ‘energy-dense’ fast foods has also been reported from Sri Lanka.75

11.2. Fatty acids and oils

South Asian diets are traditionally low in monounsaturated fatty acids (MUFA), n-3 polysaturated fatty acids (PUFAs), and high in fats, saturated fats, n-6 PUFAs and trans-fatty acids (mostly related to the widespread use of Vanaspati, a partially hydrogenated vegetable oil) and this may be associated with increased risk for cardiometabolic disorders.46,72 In addition, recent data show that high heat cooking, as practiced in most Indian households, may increase levels of trans fatty acids.70 Finally, oils with high saturated fat content often used by South Asians (clarified butter, coconut oil) which have been shown to raise LDL, may potentially increase cardiovascular risk.46

11.3. Sugar

The intake of total sugar (added sugar in preparations such as sweets, added in coffee/tea on the table and sugar sweetened beverages) has tripled worldwide during the last 50 years. The sugar consumption in India exceeds the average global annual per capita consumption.77 Intake of sugar and sugar-sweetened beverages intake among Asian Indians may contribute to the risk of abdominal obesity and insulin resistance although in absolute terms refined carbohydrates (e.g., dietary intake of polished white rice) remains the main culprit.77,78

11.4. Fruits and vegetables

The average per capita consumption of fruit and vegetables in India is about 3 servings/day,79 and even lesser in Sri Lanka and Nepal. Inverse association between intake of fruit and vegetables and blood pressure, WC, total cholesterol and low-density lipoprotein cholesterol (LDL-c) concentrations have been shown in South India.79

11.5. Proteins

Intake of protein is generally low in largely vegetarian population in India and Nepal but may be better in predominantly non-vegetarian populations in Pakistan, Sri Lanka and Bangladesh.80 Healthy dietary practices should involve reductions in refined carbohydrate intake, saturated fats, salt and added sugars, with an increased intake of intact whole grains, fruits and vegetables. Improving intake of MUFA rich foods such as nuts and oils like mustard, olive, groundnut or rice bran oil and increasing n-3 PUFAs through fatty fish for non-vegetarians and flax seeds and other sources for vegetarians.46,81 In general, refined carbohydrates should be substituted with good quality dietary protein so as to make it about 20% of total energy, as the same time increasing intake of leucine-rich foods.46,72

12. Physical activity

Asian Indians/South Asians are more sedentary, than White Caucasians.27 Importantly, nearly 90% of males and females in India are not involved in regular recreational exercise,81 while television viewing for long hours was common in all age groups. Physical inactivity is increasing in South Asia because of urbanization and mechanization. Further, as with the Europeans, lower physical activity in Asian Indians is inversely correlated with BMI, waist circumference, systolic blood pressure, and plasma glucose and insulin levels.82 In view of known ethnic differences in body composition, particularly sarcopenia and higher prevalence of insulin resistance, MetS and T2DM in younger age groups and at lower BMI in Asian Indians, international physical activity guidelines may need to be modified (increased exercise time) to reflect the ethnic phenotypic and lifestyle characteristics.83 For example, a comparative study estimated that South Asian adults needed to undertake 232 (95% CI: 200 to 268) minutes per week of physical activity to obtain the same cardio-metabolic benefits as a White European undertaking 150 min of moderate-equivalent physical activity per week. This translates to South Asians undertaking an extra 10–15 min of moderate intensity physical activity per day on top of existing recommendations.84 Finally, it is important to include resistance exercises in any exercise programs pertaining to South Asians.83

Table 2 lists randomized controlled trials in Asian Indians/south Asians with metabolic syndrome (Fig. 1). These trials incorporate a variety of approaches, including diets, physical activity, yoga and multi-component interventions. While many of these show benefits of interventions, more studies are required with innovative lifestyle-based interventions in South Asian countries. Specifically, while meagre data exists regarding structural exercise protocols in obesity, MetS and T2DM, mostly limited to migrant South Asians, more robust trials are required.

13. Socio-cultural factors

Socio-cultural and religious beliefs of South Asians impact on their diet and lifestyle, disease detection, prevention and management. South Asians are challenged by many interrelated factors that influence their food and lifestyle choices. These include their personal economic standing in society, level of education, religious beliefs, family background and traditional cultural expectations. For example, there is also tendency of south Asians to consume excess amount of sugars and carbohydrates during festivals and social engagements.77 Mothers (often
obese themselves) influence dietary choices of children, which may contribute to childhood obesity.\textsuperscript{85} Socio-cultural barriers to change included preference for work-related commitments over time for physical activity, less motivation per se to be physically active, religious and other family ceremonies/social events that invariably includes feasting and fasting which disrupts dietary behavioral change, and in married men, a total dependency on the wife for all cooking.\textsuperscript{86} Women reported fears of personal safety when going out for exercise alone, lack of acceptance of western styled clothes for physical activity, and the beliefs that women were home makers and have to provide home cooked foods.\textsuperscript{86}

The bulk of such evidence comes from studies on South Asian diaspora in several countries and included first and second-generation nationals. There is a need for a systematic understanding of the socio-cultural pressures in south Asian countries today, and how they impact on diet and lifestyle environment favoring MetS and T2DM.

14. Genetics and epigenetics

Studies among South Asians have also suggested the contribution of environment to an already obesogenic genotype.\textsuperscript{87} However, despite the large heritability component, search for precise genetic markers and mechanisms responsible for adiposity have identified genetic polymorphisms that explain only a small proportion of the adiposity variance. Some loci such as FTO and near-MC4R region are well known to be associated with obesity, and this has been replicated in numerous studies. Overall, with dramatic reduction in costs of genotyping and next-generation sequencing, larger studies focusing on homogenous population subgroups are possible, both among native and South Asian diaspora and would greatly enhance our understanding of T2DM in this population.

15. Conclusions

This review systematically addresses the many etiopathological factors that contribute to MetS and T2DM in context of adiposity in South Asians. We highlight the role of adipose tissue distribution focusing on ectopic fat, diet, other lifestyle factors, an altered hormonal and systemic inflammatory milieu, potential genetic/epigenetic influences on the increased risk of MetS. Clearly, the problem has multi-factorial antecedents. Efforts to address its management and combat its increasing prevalence would need to embrace a life course approach and an integrated approach to the problem of

<table>
<thead>
<tr>
<th>Study name/author</th>
<th>Year</th>
<th>N</th>
<th>Design</th>
<th>Duration</th>
<th>Disease/condition</th>
<th>Type of intervention</th>
<th>Result/observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manchanda et al.\textsuperscript{88}</td>
<td>2013</td>
<td>101</td>
<td>RCT</td>
<td>12 months</td>
<td>MetS</td>
<td>Yoga vs. usual care</td>
<td>Significant improvement in HDL-c among cases vs. controls, marginal significant improvement in WC</td>
</tr>
<tr>
<td>Nigam et al.\textsuperscript{89}</td>
<td>2013</td>
<td>93</td>
<td>RCT</td>
<td>6 months</td>
<td>NAFLD</td>
<td>Canola oil vs. olive oil vs. other oils Diet including pistachio nuts vs. control</td>
<td>Significant improvements in grading of fatty liver, liver span, insulin resistance and lipids with use of canola and olive oil</td>
</tr>
<tr>
<td>Gulati et al.\textsuperscript{90}</td>
<td>2014</td>
<td>60</td>
<td>RCT</td>
<td>24 weeks</td>
<td>Mets</td>
<td>Yoga vs. stretching</td>
<td>Significant improvement in FBG and transient improvements at 6 months for insulin, HbA1c and HDL-c.</td>
</tr>
<tr>
<td>Kanaya et al.\textsuperscript{91}</td>
<td>2014</td>
<td>180</td>
<td>RCT</td>
<td>48 weeks</td>
<td>MetS</td>
<td>High protein meal replacement vs. equicaloric diet</td>
<td>Improvements in all MetS components and hepatic transaminases in protein replacement group</td>
</tr>
<tr>
<td>Gulati et al.\textsuperscript{92}</td>
<td>2017</td>
<td>122</td>
<td>RCT</td>
<td>12 weeks</td>
<td>Overweight/obese</td>
<td>Cinnamon vs. placebo</td>
<td>Weight loss, improvement of skin fold thickness, decreased clustering of MetS risk factors</td>
</tr>
<tr>
<td>Jain et al.\textsuperscript{93}</td>
<td>2017</td>
<td>116</td>
<td>RCT</td>
<td>16 weeks</td>
<td>MetS</td>
<td>Intensive vs. standard intervention (exercise, diet)</td>
<td>Significant improvement in HDL-c among cases vs. controls, marginal significant improvement in WC</td>
</tr>
<tr>
<td>Shrivastava et al.\textsuperscript{94}</td>
<td>2017</td>
<td>267</td>
<td>RCT</td>
<td>6 months</td>
<td>Overweight worksite employees</td>
<td>Diet</td>
<td>Significant improvement in HDL-c among cases vs. controls, marginal significant improvement in WC</td>
</tr>
</tbody>
</table>

Fig. 1. A Schematic Diagram showing Interlinking Factors that Promote Metabolic Syndrome in South Asians.
chronic disease. More research is needed to develop low cost and culturally appropriate lifestyle intervention to combat MetS to prevent T2DM in South Asians.

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