Journal of Diabetes and Its Complications 32 (2018) 1068–1075

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Body fat, metabolic syndrome and hyperglycemia in South Asians

A. Misra [a,b,c,*], Mario J. Soares [d], Viswanathan Mohan [e], Shajith Anoop [a,b], Vishnu Abhishek [e], Ruchi Vaidya [f], Rajendra Pradeepa [g]

[a] Centre of Nutrition & Metabolic Research (C-NET), National Diabetes, Obesity and Cholesterol Foundation (N-DOC), SDA, New Delhi, India
[b] Diabetes Foundation (India), SDA, New Delhi, India
[c] Fortis C-DOC Centre of Excellence for Diabetes, Metabolic Diseases and Endocrinology, Chirag Enclave, Nehru Place, New Delhi, India
[d] School of Public Health, Faculty of Health Sciences, Curtin University, Perth, Western Australia, Australia
[e] Department of Epidemiology & Diabetology, Madras Diabetes Research Foundation & Dr Mohan's Diabetes Specialties Centre, Chennai, India
[f] Genetics of Obesity and Related Traits Program, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[g] Department of Foods Nutrition & Dietetics Research, Madras Diabetes Research Foundation, Chennai, Tamil Nadu, India

A R T I C L E I N F O

Article history:
Received 30 March 2018
Received in revised form 31 July 2018
Accepted 2 August 2018
Available online 4 August 2018

Keywords:
Metabolic syndrome
Obesity
Ectopic fat
Asian Indians
South Asians
Diabetes

A B S T R A C T

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.

© 2018 Published by Elsevier Inc.

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).[1] 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.[2–4]

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 an ethnic grouping 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.

Conflicts of interest: none.

* Corresponding author at: Fortis C-DOC Centre of Excellence for Diabetes, Metabolic Diseases and Endocrinology, Chirag Enclave, Nehru Place, New Delhi, India.
E-mail address: anoopmisra@gmail.com (A. Misra).

https://doi.org/10.1016/j.jdiacomp.2018.08.001
1056-8727/© 2018 Published by Elsevier Inc.

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.[5] 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.[6] 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[7] and immigrant Asian Indians in USA.[8] 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.[9] Rajak et al.[10] 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/m^2 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.[11] 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/m^2 in Indian populations compared to 25 kg/m^2 in Europeans.[12] Similarly, waist circumference cut-offs for south Asians are lower (≤80 cm in women and ≤90 cm in men) based on data from India[3] and other countries.[11]

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/m^2 and that for obesity was ≥25 kg/m^2.[13] These and other data prompted the Indian Consensus Group in 2009 to define BMI levels of 23–24.9 kg/m^2 for overweight and ≥25 kg/m^2 for obesity.[4] In 2013, a review of recent studies conducted on Asian-Americans by Hsu et al.[14] 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/m^2 is appropriate for Asian populations residing in USA, and the same has been stated in position statement for 2015 by American Diabetes Association.[15] Importantly, lower BMI cut-points for metabolic surgery for obesity for Asian Americans *vs.* other ethnicities (27.5 *vs.* 30 kg/m^2, respectively) have recently been emphasized.[16]

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.[17] 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 26.1%, 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.[18] 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%).[19] 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%).[9,20] 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).[21] 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]

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.[23] However, some authors have shown that blood glucose level[24] or glucose tolerance[25] 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.[12] In Asian Indians, a higher prevalence of abdominal obesity is noted even at low levels of BMI.[4,26] Obesity in south Asians is featured by high body fat percentage,[4,26] increased total abdominal fat, intra-abdominal visceral fat, and truncal fat, in comparison to white Caucasians.[27] 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%),[43]

Table 1
Body Fat and Ectopic fat Depots in South Asians: Anatomical Comparison to Whites and Other Ethnic Groups@ and Relationship to Metabolic Dysregulation.

Variable	Difference relative to White Caucasians/other ethnicities[a]	Comment	Reference
Total body fat	Increased	Relevance of excess total body fat alone to insulin resistance is not clear	Deurenberg-Yap et al.,[6], Gao et al.[28], Anand et al.[29b], Lear et al.[30c]
Truncal and abdominal subcutaneous fat[b]	Increased, Deep subcutaneous abdominal fat more relevant to metabolism?	Related to insulin sensitivity and metabolic syndrome, diabetes.	Lear et al.[30c], Goel et al.[31], Chandalia et al.[32d], Chandalia et al.[33b], Marinou et al.[34e], Eastwood et al.[35f], Anand et al.[29g]
Intra-abdominal visceral fat	Increased	Related to decreased glucose disposal rates and dyslipidemia. Gender differences.	Raji et al.[36h], Lear et al.[30c]
Thigh subcutaneous adipose tissue and skeletal muscle lipids (intra-myocellular triglycerides)	Increased	Thigh subcutaneous tissue protective for diabetes Intramyocellular triglycerides not related to insulin resistance? More data needed	Eastwood et al.[37i], Forouhi et al.[38h], Sinha et al.[39]
Hepatic fat (non-alcoholic fatty liver disease)	Increased	Related to increased insulin resistance and pro-inflammatory cytokines. Association with CVD.	Petersen et al.[40b]
Epicardial fat	Conflicting data	Further research required. Associated with coronary artery calcium.	Adams et al.[41g], Garg et al.[42j]
Pancreatic fat (non-alcoholic fatty pancreas disease)	No comparative data. Increased pancreatic volume (surrogate of excess fat) shown in Asian Indians	Research needed if related to insulin secretion and insulin resistance	Misra et al.[43]
Brown adipose tissue (BAT)	Lesser BAT volume	Conflicting data on BAT activity Lower related to less resting energy expenditure (? predisposes to obesity and diabetes)	Bakker et al.[44b], Admiraal et al.[45b]
Subcutaneous adipocytes	Larger adipocyte size in trunk, increased small adipocyte number due to maturation arrest?	Size inversely related to glucose disposal rate. Increase inflammation in subcutaneous adipose tissue in Asian Indians *vs.* Whites regardless of total adipocyte mass	Chandalia et al.[33b], Anand et al.[29g]

Adapted from Gulati and Misra[46] and other reviews.[26,27]
[a] 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.[42] compared Asian Indians with whites, blacks, Latinos, and Chinese Americans.
[b] Adjusted/matched for BMI.
[c] Adjusted for age, income, smoking status, and BMI.
[d] Matched for BMI, body fat and age.
[e] Matched for subcutaneous fat, age and gender.
[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.

have high glucagon levels[47] 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.[33]

Irrespective of obesity, larger abdominal adipocyte size predicts insulin resistance as well as T2DM independent of insulin resistance.[48] 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.[29] 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.[49] 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.[50]

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[31] phosphorous magnetic resonance spectroscopy (MRS), significant derangements of hepatic gluconeogenesis pathway was shown in normo-glycemic, normo-lipidemic and normotensive Asian Indians with NAFLD.[51] 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.[40] 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-a-vis* insulin resistance and MetS and T2DM. A preliminary communication has reported a cut-off of 6.2% to define excess pancreatic fat.[52] 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 in T2DM in South Asians,[53] although there is paucity of research data. In an MRI-based case–control study on non-obese (BMI < 25 kg/m^2) 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.[43]

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.[54] 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 mechanism(s) other that mediated through IMCL is/are responsible for insulin resistance in South Asians.[38] 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-abdominal visceral fat mass and reduction of muscle mass and strength and bone mass density.[55] Recent studies have shown that obese individuals have lower maximal strength when the latter is expressed relative to body mass. In addition, adiposity is shown to cause a loading effect on skeletal muscles of the lower limbs among both younger and older adults.[56] BMI-adjusted lean mass was inversely associated with MetS among community-dwelling participants in Australia and South Korea although the association did not reach significance among South Koreans.[57]

The body composition in South Asian men and women consistently shows significantly lesser lean mass than Whites.[27] Indeed, one study showed greater pre-sarcopenia in Asian Indians with diabetes compared to age and gender matched controls without diabetes.[58] This unique phenotype (high body fat-low muscle mass-low BMI) contributes to insulin resistance and T2DM in South Asians. A recent study from the UK Biobank showed lower grip strength (indicative of sarcopenia) among South Asians as compared to whites and blacks, which was related to higher prevalence of T2DM in the former.[59] In this respect, it is important to note that in obese German adults, grip strength was an indicator of whole body strength, as the relationship between obesity and strength of the upper *versus* lower extremities differed.[60] In a study done on Swedish and Indian men, the latter had lower lean mass, higher body adiposity, and, in particular, lesser lean mass in legs, however, lower extremity strength was not evaluated.[61] The reason for the low muscle mass in Asian Indians is unclear. Overall, it appears that low dietary protein intake, physical inactivity and fetal undernutrition may contribute singly or in combination.[46] In addition, genetic effects cannot be ruled out, and in this context, genetic polymorphisms in the *myostatin* gene have been shown to play a role.[62]

7. Early loss of beta cell function

While increased insulin resistance among South Asians has been recognized,[63] 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.[64] 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.[65] 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.[66] 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.[67] 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.[40] 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.[68]

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.[69]

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 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 cardio-metabolic 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.[71] 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 (MUFAs), *n*-3 polyunsaturated 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.[46,73] In addition, recent data show that high heat cooking, as practiced in most Indian households, may increase levels of trans fatty acids.[76] 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.[46]

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.[46,80] 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 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

Table 2
Lifestyle Intervention Studies Among Asian Indians with Metabolic Syndrome and other Metabolic Abnormalities.

Study name/author	Year	*N*	Design	Duration	Disease/condition	Type of intervention	Result/observations
Manchanda et al.[88]	2013	101	RCT	12 months	MetS	Yoga *vs.* usual care	Significant improvement in HDL-c among cases *vs.* controls, marginal significant improvement in WC
Nigam et al.[89]	2013	93	RCT	6 months	NAFLD	Canola oil *vs.* olive oil *vs.* other oils	Significant improvements in grading of fatty liver, liver span, insulin resistance and lipids with use of canola and olive oil
Gulati et al.[90]	2014	60	RCT	24 weeks	Mets	Diet including pistachio nuts *vs.* control	Significant improvements among intervention group for waist circumference, FBG, TC, LDL-c, hs-CRP, TNF-α, FFA, and adiponectin
Kanaya et al.[91]	2014	180	RCT	48 weeks	MetS	Yoga *vs.* stretching	Significant improvement in FBG and transient improvements at 6 months for insulin, HbA1c and HDL-c.
Gulati et al.[92]	2017	122	RCT	12 weeks	Overweight/obese	High protein meal replacement *vs.* equicaloric diet	Improvements in all MetS components and hepatic transaminases in protein replacement group
Jain et al.[93]	2017	116	RCT	16 weeks	MetS	Cinnamon *vs.* placebo	Significant improvement in all components of MetS and skinfold thickness in intervention but not in control group
Shrivastava et al.[94]	2017	267	RCT	6 months	Overweight worksite employees	Intensive *vs.* standard intervention (exercise, diet)	Weight loss, improvement of skin fold thickness, decreased clustering of MetS risk factors

obese themselves) influence dietary choices of children, which may contribute to childhood obesity.[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.[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.[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.[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

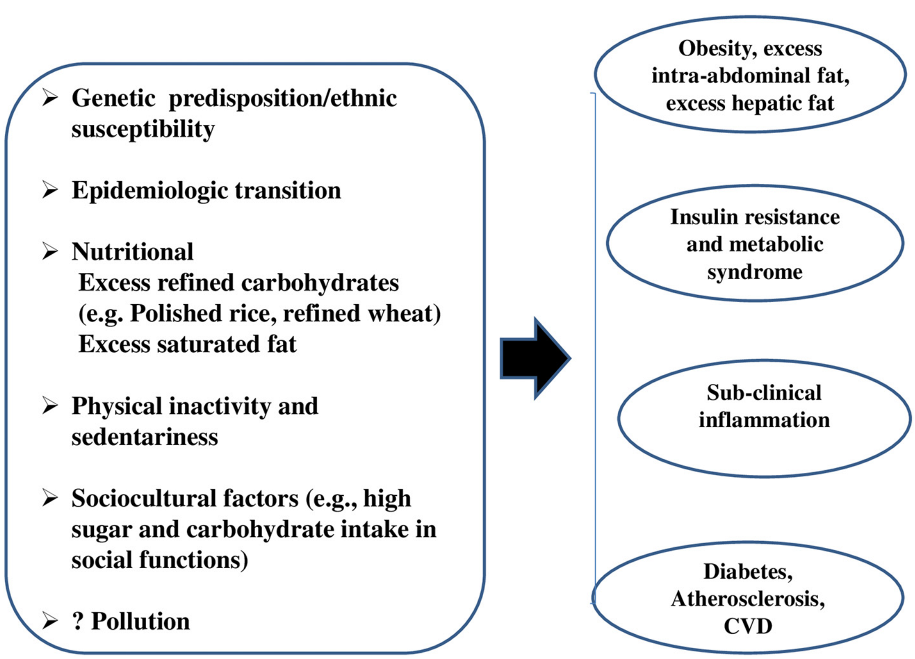

Fig. 1. A Schematic Diagram showing Interlinking Factors that Promote Metabolic Syndrome in South Asians.

chronic disease. More research is needed to develop low cost and culturally appropriate lifestyle intervention to combat MetS to prevent T2DM in South Asians.

Acknowledgement

We wish to thank Dr. M. Balasubramanyam, Dean of Research Studies & Mrs. SudhaVasudevan, Sr. Scientist & Head, Department of Foods, Nutrition &Dietetics Research (FNDR), Madras Diabetes Research Foundation (MDRF), Chennai, India for their academic inputs towards this article.

References

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640-5.
2. Misra A, Vikram NK. Clinical and pathophysiological consequences of abdominal adiposity and abdominal adipose tissue depots. Nutrition 2003;19:457-66.
3. Misra A, Vikram NK, Gupta R, Pandey RM, Wasir JS, Gupta VP. Waist circumference cutoff points and action levels for Asian Indians for identification of abdominal obesity. Int J Obes (Lond) 2006;30:106-11.
4. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India 2009;57:163-70.
5. Tillin T, Forouhi N, Johnston DG, McKeigue PM, Chaturvedi N, Godsland IF. Metabolic syndrome and coronary heart disease in South Asians, African-Caribbeans and White Europeans: a UK population-based cross-sectional study. Diabetologia 2005;48:649-56.
6. Deurenberg-Yap M, Schmidt G, van Staveren WA, Deurenberg P. The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore. Int J Obes Relat Metab Disord 2000;24:1011-7.
7. Dudeja V, Misra A, Pandey RM, Devina G, Kumar G, Vikram NK. BMI does not accurately predict overweight in Asian Indians in northern India. Br J Nutr 2001;86:105-12.
8. Banerji MA, Faridi N, Atluri R, Chaiken RL, Lebovitz HE. Body composition, visceral fat, leptin, and insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999;84:137-44.
9. Chow CK, Naidu S, Raju K, Raju R, Joshi R, Sullivan D, et al. Significant lipid, adiposity and metabolic abnormalities amongst 4535 Indians from a developing region of rural Andhra Pradesh. Atherosclerosis 2008;196:943-52.
10. Razak F, Anand SS, Shannon H, Vuksan V, Davis B, Jacobs R, et al. Defining obesity cut points in a multiethnic population. Circulation 2007;115:2111-8.
11. Bodicoat DH, Gray LJ, Henson J, Webb D, Guru A, Misra A, et al. Body mass index and waist circumference cut-points in multi-ethnic populations from the UK and India: the ADDITION-Leicester, Jaipur heart watch and New Delhi cross-sectional studies. PLoS One 2014;9, e90813.
12. Nakagami T, Qiao Q, Carstensen B, Nhr-Hansen C, Hu G, Tuomilehto J, et al. Age, body mass index and type 2 diabetes-associations modified by ethnicity. Diabetologia 2003;46:1063-70.
13. World Health Organization, International Association of Study of Obesity, International Obesity Task Force. *The Asia-Pacific Perspective. Redefining Obesity and Its Treatment*. International Diabetes Institute, Health Communications Australia Pty Ltd. 2000. Available at http://www.obesityasiapacific.com/default.htm.
14. Hsu WC, Araneta MR, Kanaya AM, Chiang JL, Fujimoto W. BMI cut points to identify at-risk Asian Americans for type 2 diabetes screening. Diabetes Care 2015;38:150-8.
15. American Diabetes Association. Standards for medical care in diabetes. Diabetes Care 2015;38:S1-S94.
16. American Diabetes Association. Standards for medical care in diabetes. Diabetes Care 2018;41:S66.
17. Misra A, Tandon N, Ebrahim S, Sattar N, Alam D, Shrivastava U, et al. Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: current status and future directions. BMJ 2017;357:j1420.
18. Aryal N, Wasti SP. The prevalence of metabolic syndrome in South Asia: a systematic review. Int J Diabetes Dev Ctries 2016;36:255-62.
19. Ranasinghe P, Mathangasinghe Y, Jayawardena R, Hills AP, Misra A. Prevalence and trends of metabolic syndrome among adults in the Asia-Pacific region: a systematic review. BMC Public Health 2017;17:101.
20. Ravikiran M, Bhansali A, Ravikumar P, Bhansali S, Dutta P, Thakur JS, et al. Prevalence and risk factors of metabolic syndrome among Asian Indians: a community survey. Diabetes Res Clin Pract 2010;89:181-8.
21. Flowers E, Molina C, Mathur A, Prasad M, Abrams L, Sathe A, et al. Prevalence of metabolic syndrome in South Asians residing in the United States. Metab Syndr Relat Disord 2010;8:417-23.
22. Rajpathak SN, Gupta LS, Waddell EN, Upadhyay UD, Wildman RP, Kaplan R, et al. Elevated risk of type 2 diabetes and metabolic syndrome among Asians and South Asians: results from the 2004 New York City HANES. Ethn Dis 2010;20:225-30.
23. Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs Framingham risk score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 2005;165:2644-50.
24. Nichols GA, Moler EJ. Diabetes incidence for all possible combinations of metabolic syndrome components. Diabetes Res Clin Pract 2010;90:115-21.
25. Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio heart study. Diabetes Care 2003;26:3153-9.
26. Misra A, Vikram NK. Insulin resistance syndrome (metabolic syndrome) and obesity in Asian Indians: evidence and implications. Nutrition 2004;20:482-91.
27. Misra A, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. Int J Obes (Lond) 2011;35:167-87.
28. Gao H, Salim A, Lee J, Tai ES, van Dam RM. Can body fat distribution, adiponectin levels and inflammation explain differences in insulin resistance between ethnic Chinese, Malays and Asian Indians? Int J Obes (Lond) 2012;36:1086-93.
29. Anand SS, Tarnopolsky MA, Rashid S, Schulze KM, Desai D, Mente A, et al. Adipocyte hypertrophy, fatty liver and metabolic risk factors in South Asians: the Molecular Study of Health and Risk in Ethnic Groups (mol-SHARE). PLoS One 2011;6, e22112.
30. Lear SA, Chockalingam A, Kohli S, Richardson CG, Humphries KH. Elevation in cardiovascular disease risk in South Asians is mediated by differences in visceral adipose tissue. Obesity (Silver Spring) 2012;20:1293-300.
31. Goel K, Misra A, Vikram NK, Poddar P, Gupta N. Subcutaneous abdominal adipose tissue is associated with the metabolic syndrome in Asian Indians independent of intra-abdominal and total body fat. Heart 2010;96:579-83.
32. Chandalia M, Abate N, Garg A, Stray-Gundersen J, Grundy SM. Relationship between generalized and upper body obesity to insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999;84:2329-35.
33. Chandalia M, Lin P, Seenivasan T, Livingston EH, Snell PG, Grundy SM, et al. Insulin resistance and body fat distribution in South Asian men compared to Caucasian men. PLoS One 2007;2, e812.
34. Marinou K, Hodson L, Vasan SK, Fielding BA, Banerjee R, Brismar K, et al. Structural and functional properties of deep abdominal subcutaneous adipose tissue explain its association with insulin resistance and cardiovascular risk in men. Diabetes Care 2014;37:821-9.
35. Eastwood SV, Tillin T, Dehbi HM, Wright A, Forouhi NG, Godsland I, et al. Ethnic differences in associations between fat deposition and incident diabetes and underlying mechanisms: the SABRE study. Obesity (Silver Spring) 2015;23:699-706.
36. Raji A, Seely EW, Arky RA, Simonson DC. Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 2001;86:5366-71.
37. Eastwood SV, Tillin T, Wright A, Mayet J, Godsland I, Forouhi NG, et al. Thigh fat and muscle each contribute to excess cardiometabolic risk in South Asians, independent of visceral adipose tissue. Obesity (Silver Spring) 2014;22:2071-9.
38. Forouhi NG, Jenkinson G, Thomas EL, Mullick S, Mierisova S, Bhonsle U, et al. Relation of triglyceride stores in skeletal muscle cells to central obesity and insulin sensitivity in European and South Asian men. Diabetologia 1999;42:932-5.
39. Sinha S, Misra A, Rathi M, Kumar V, Pandey RM, Luthra K, et al. Proton magnetic resonance spectroscopy and biochemical investigation of type 2 diabetes mellitus in Asian Indians: observation of high muscle lipids and C-reactive protein levels. Magn Reson Imaging 2009;27:94-100.
40. Petersen KF, Dufour S, Feng J, Befroy D, Dziura J, Dalla Man C, et al. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. Proc Natl Acad Sci U S A 2006;103:18273-7.
41. Adams DB, Narayan O, Munnur RK, Cameron JD, Wong DT, Talman AH, et al. Ethnic differences in coronary plaque and epicardial fat volume quantified using computed tomography. Int J Cardiovasc Imaging 2017;33:241-9.
42. Garg SK, Lin F, Kandula N, Ding J, Carr J, Allison M, et al. Ectopic fat depots and coronary artery calcium in South Asians compared with other racial/ethnic groups. J Am Heart Assoc 2016;5.
43. Misra A, Anoop S, Gulati S, Mani K, Bhatt SP, Pandey RM. Body fat patterning, hepatic fat and pancreatic volume of non-obese Asian Indians with type 2 diabetes in north India: a case-control study. PLoS One 2015;10, e0140447.
44. Bakker LE, Boon MR, van der Linden RA, Arias-Bouda LP, van Klinken JB, Smit F, et al. Brown adipose tissue volume in healthy lean south Asian adults compared with white Caucasians: a prospective, case-controlled observational study. Lancet Diabetes Endocrinol 2014;2:210-7.
45. Admiraal WM, Verberne HJ, Karamat FA, Soeters MR, Hoekstra JB, Holleman F. Cold-induced activity of brown adipose tissue in young lean men of South-Asian and European origin. Diabetologia 2013;56:2231-7.
46. Gulati S, Misra A. Abdominal obesity and type 2 diabetes in Asian Indians: dietary strategies including edible oils, cooking practices and sugar intake. Eur J Clin Nutr 2017;71:850-7.
47. Anoop S, Misra A, Bhatt SP, Gulati S, Mahajan H, Prabakaran G. High plasma glucagon levels correlate with waist-to-hip ratio, suprailiac skinfold thickness, and deep subcutaneous abdominal and intraperitoneal adipose tissue depots in nonobese Asian Indian males with type 2 diabetes in North India. J Diabetes Res 2017;2017:2376016.
48. Weyer C, Foley JE, Bogardus C, Tataranni PA, Pratley RE. Enlarged subcutaneous abdominal adipocyte size, but not obesity itself, predicts type II diabetes independent of insulin resistance. Diabetologia 2000;43:1498-506.
49. Skurk T, Alberti-Huber C, Herder C, Hauner H. Relationship between adipocyte size and adipokine expression and secretion. J Clin Endocrinol Metab 2007;92:1023-33.
50. Munoz A, Abate N, Chandalia M. Adipose tissue collagen and inflammation in nonobese Asian Indian men. J Clin Endocrinol Metab 2013;98:E1360-3.
51. Sharma R, Sinha S, Danishad KA, Vikram NK, Gupta A, Ahuja V, et al. Investigation of hepatic gluconeogenesis pathway in non-diabetic Asian Indians with non-alcoholic fatty liver disease using in vivo ((31)P) phosphorus magnetic resonance spectroscopy. Atherosclerosis 2009;203:291-7.

52. Singh RG, Yoon HD, Wu LM, Lu J, Plank LD, Petrov MS. Ectopic fat accumulation in the pancreas and its clinical relevance: a systematic review, meta-analysis, and meta-regression. Metabolism 2017;69:1-13.
53. Bhopal RS. A four-stage model explaining the higher risk of type 2 diabetes mellitus in South Asians compared with European populations. Diabet Med 2013;30:35-42.
54. Misra A, Sinha S, Kumar M, Jagannathan NR, Pandey RM. Proton magnetic resonance spectroscopy study of soleus muscle in non-obese healthy and type 2 diabetic Asian Northern Indian males: high intramyocellular lipid content correlates with excess body fat and abdominal obesity. Diabet Med 2003;20:361-7.
55. Tomlinson DJ, Erskine RM, Winwood K, Morse CI, Onambele GL. The impact of obesity on skeletal muscle architecture in untrained young vs. old women. J Anat 2014;225:675-84.
56. Otten L, Bosy-Westphal A, Ordemann J, Rothkegel E, Stobaus N, Elbelt U, et al. Abdominal fat distribution differently affects muscle strength of the upper and lower extremities in women. Eur J Clin Nutr 2017;71:372-6.
57. Scott D, Park MS, Kim TN, Ryu JY, Hong HC, Yoo HJ, et al. Associations of low muscle mass and the metabolic syndrome in Caucasian and Asian middle-aged and older adults. J Nutr Health Aging 2016;20:248-55.
58. Anbalagan VP, Venkataraman V, Pradeepa R, Deepa M, Anjana RM, Mohan V. The prevalence of presarcopenia in Asian Indian individuals with and without type 2 diabetes. Diabetes Technol Ther 2013;15:768-75.
59. Ntuk UE, Celis-Morales CA, Mackay DF, Sattar N, Pell JP, Gill JMR. Association between grip strength and diabetes prevalence in black, South-Asian, and White European ethnic groups: a cross-sectional analysis of 418 656 participants in the UK Biobank study. Diabet Med 2017;34:1120-8.
60. Scott D, Blizzard L, Fell J, Jones G. Prospective associations between ambulatory activity, body composition and muscle function in older adults. Scand J Med Sci Sports 2011;21:e168-75.
61. Chowdhury B, Lantz H, Sjostrom L. Computed tomography-determined body composition in relation to cardiovascular risk factors in Indian and matched Swedish males. Metabolism 1996;45:634-44.
62. Bhatt SP, Nigam P, Misra A, Guleria R, Luthra K, Jain SK, et al. Association of the Myostatin gene with obesity, abdominal obesity and low lean body mass and in non-diabetic Asian Indians in north India. PLoS One 2012;7, e40977.
63. Mohan V, Sharp PS, Cloke HR, Burrin JM, Schumer B, Kohner EM. Serum immunoreactive insulin responses to a glucose load in Asian Indian and European type 2 (non-insulin-dependent) diabetic patients and control subjects. Diabetologia 1986;29:235-7.
64. Staimez LR, Weber MB, Ranjani H, Ali MK, Echouffo-Tcheugui JB, Phillips LS, et al. Evidence of reduced beta-cell function in Asian Indians with mild dysglycemia. Diabetes Care 2013;36:2772-8.
65. Priya MM, Amutha A, Pramodkumar TA, Ranjani H, Jebarani S, Gokulakrishnan K, et al. Beta-cell function and insulin sensitivity in normal glucose-tolerant subjects stratified by 1-hour plasma glucose values. Diabetes Technol Ther 2016;18:29-33.
66. Sulistyoningrum DC, Gasevic D, Lear SA, Ho J, Mente A, Devlin AM. Total and high molecular weight adiponectin and ethnic-specific differences in adiposity and insulin resistance: a cross-sectional study. Cardiovasc Diabetol 2013;12:170.
67. Parvaresh Rizi E, Teo Y, Leow MK, Venkataraman K, Khoo EY, Yeo CR, et al. Ethnic differences in the role of adipocytokines linking abdominal adiposity and insulin sensitivity among Asians. J Clin Endocrinol Metab 2015;100:4249-56.
68. Webb DR, Khunti K, Chatterjee S, Jarvis J, Davies MJ. Adipocytokine associations with insulin resistance in British South Asians. J Diabetes Res 2013;2013:561016.
69. Ward AM, Fall CH, Stein CE, Kumaran K, Veena SR, Wood PJ, et al. Cortisol and the metabolic syndrome in South Asians. Clin Endocrinol (Oxf) 2003;58:500-5.
70. Deepa M, Farooq S, Datta M, Deepa R, Mohan V. Prevalence of metabolic syndrome using WHO, ATPIII and IDF definitions in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-34). Diabetes Metab Res Rev 2007;23:127-34.
71. Radhika G, Van Dam RM, Sudha V, Ganesan A, Mohan V. Refined grain consumption and the metabolic syndrome in urban Asian Indians (Chennai Urban Rural Epidemiology Study 57). Metabolism 2009;58:675-81.
72. Sowmya N, Lakshmipriya N, Arumugam K, Venkatachalam S, Vijayalakshmi P, Ruchi V, et al. Comparison of dietary profile of a rural south Indian population with the current dietary recommendations for prevention of non-communicable diseases (CURES 147). Indian J Med Res 2016;144:112-9.
73. Radhika G, Sathya RM, Ganesan A, Saroja R, Vijayalakshmi P, Sudha V, et al. Dietary profile of urban adult population in south India in the context of chronic disease epidemiology (CURES-68). Public Health Nutr 2011;14:591-8.
74. Mohan V, Radhika G, Sathya RM, Tamil SR, Ganesan A, Sudha V. Dietary carbohydrates, glycaemic load, food groups and newly detected type 2 diabetes among urban Asian Indian population in Chennai, India (Chennai Urban Rural Epidemiology Study 59). Br J Nutr 2009;102:1498-506.
75. Jayawardena R, Byrne NM, Soares MJ, Katulanda P, Hills AP. Food consumption of Sri Lankan adults: an appraisal of serving characteristics. Public Health Nutr 2013;16:653-8.
76. Bhardwaj S, Passi SJ, Misra A, Pant KK, Anwar K, Pandey RM, et al. Effect of heating/reheating of fats/oils, as used by Asian Indians, on trans fatty acid formation. Food Chem 2016;212:663-70.
77. Gulati S, Misra A. Sugar intake, obesity, and diabetes in India. Nutrients 2014;6:5955-74.
78. Radhika G, Ganesan A, Sathya RM, Sudha V, Mohan V. Dietary carbohydrates, glycemic load and serum high-density lipoprotein cholesterol concentrations among south Indian adults. Eur J Clin Nutr 2009;63:413-20.
79. Radhika G, Sudha V, Mohan Sathya R, Ganesan A, Mohan V. Association of fruit and vegetable intake with cardiovascular risk factors in urban south Indians. Br J Nutr 2008;99:398-405.
80. Misra A, Sharma R, Gulati S, Joshi SR, Sharma V, Ghafoorunissa, et al. Consensus dietary guidelines for healthy living and prevention of obesity, the metabolic syndrome, diabetes, and related disorders in Asian Indians. Diabetes Technol Ther 2011;13:683-94.
81. Anjana RM, Pradeepa R, Das AK, Deepa M, Bhansali A, Joshi SR, et al. Physical activity and inactivity patterns in India - results from the ICMR-INDIAB study (phase-1) [ICMR-INDIAB-5]. Int J Behav Nutr Phys Act 2014;11:26.
82. Hayes L, White M, Unwin N, Bhopal R, Fischbacher C, Harland J, et al. Patterns of physical activity and relationship with risk markers for cardiovascular disease and diabetes in Indian, Pakistani, Bangladeshi and European adults in a UK population. J Public Health Med 2002;24:170-8.
83. Misra A, Nigam P, Hills AP, Chadha DS, Sharma V, Deepak KK, et al. Consensus physical activity guidelines for Asian Indians. Diabetes Technol Ther 2012;14:83-98.
84. Iliodromiti S, Ghouri N, Celis-Morales CA, Sattar N, Lumsden MA, Gill JM. Should physical activity recommendations for South Asian adults be ethnicity-specific? Evidence from a cross-sectional study of South Asian and White European men and women. PLoS One 2016;11, e0160024.
85. Gulati S, Misra A, Colles SL, Kondal D, Gupta N, Goel K, et al. Dietary intakes and familial correlates of overweight/obesity: a four-cities study in India. Ann Nutr Metab 2013;62:279-90.
86. Patel N, Ferrer HB, Tyrer F, Wray P, Farooqi A, Davies MJ, et al. Barriers and facilitators to healthy lifestyle changes in minority ethnic populations in the UK: a narrative review. J Racial Ethn Health Disparities 2017;4:1107-19.
87. Moore SC, Gunter MJ, Daniel CR, Reddy KS, George PS, Yurgalevitch S, et al. Common genetic variants and central adiposity among Asian-Indians. Obesity (Silver Spring) 2012;20:1902-8.
88. Manchanda S, Mehrotra UC, Makhija A, Mohanty A, Dhawan S, Sawhney JPS. Reversal of early Atherosclerosis in metabolic syndrome by yoga-a randomized controlled trial. J Yoga Phys Ther 2013;3:1.
89. Nigam P, Bhatt S, Misra A, Chadha DS, Vaidya M, Dasgupta J, et al. Effect of a 6-month intervention with cooking oils containing a high concentration of monounsaturated fatty acids (olive and canola oils) compared with control oil in male Asian Indians with nonalcoholic fatty liver disease. Diabetes Technol Ther 2014;16:255-61.
90. Gulati S, Misra A, Pandey RM, Bhatt SP, Saluja S. Effects of pistachio nuts on body composition, metabolic, inflammatory and oxidative stress parameters in Asian Indians with metabolic syndrome: a 24-wk, randomized control trial. Nutrition 2014;30:192-7.
91. Kanaya AM, Araneta MR, Pawlowsky SB, Barrett-Connor E, Grady D, Vittinghoff E, et al. Restorative yoga and metabolic risk factors: the Practicing restorative yoga vs. stretching for the metabolic syndrome (PRYSMS) randomized trial. J Diabetes Complications 2014;28:406-12.
92. Gulati S, Misra A, Tiwari R, Sharma M, Pandey RM, Yadav CP. Effect of high-protein meal replacement on weight and cardiometabolic profile in overweight/obese Asian Indians in north India. Br J Nutr 2017;117:1531-40.
93. Gupta Jain S, Puri S, Misra A, Gulati S, Mani K. Effect of oral cinnamon intervention on metabolic profile and body composition of Asian Indians with metabolic syndrome: a randomized double-blind control trial. Lipids Health Dis 2017;16:113.
94. Shrivastava U, Fatma M, Mohan S, Singh P, Misra A. Randomized control trial for reduction of body weight, body fat patterning, and cardiometabolic risk factors in overweight worksite employees in Delhi, India. J Diabetes Res 2017;2017:7254174.