ISSUE 09 | VOLUME - 23 | SEPTEMBER 2018

IMPA NEWS

THE OFFICIAL NEWS LETTER OF THE INDEPENDENT MEDICAL PRACTITIONERS ASSOCIATION

IMPA News

The IMPA Journal 2018 will be released at the AGM to be held on Sunday 16th December 2018. Members are requested to send in articles to be included in this Journal.

The 31st Annual Conference of the OPA "Innovation Digitalization" was successfully held on 26th & 27th September 2018 at the Cinnamon Lakeside Hotel, Colombo.

The Palliative Care Association of Sri Lanka (PCASL) is commemorating the World Hospice and Palliative Care Day 2018 on Saturday 13th October 2018 at the Lanka Hospital Auditorium at which the Mallika Rani Khoja Oration will be delivered.

The Foundation sessions of the SLMA will be held on Thursday 18th and Friday 19th October 2018. The IMPA Patron Prof. Lalitha Mendis will deliver the Wijerama Oration on "Medical Education in Sri Lanka".

The College of Medical Administrators of Sri Lanka has invited three IMPA members each worth (Rs.19000/-) for the conference on the "Fourth Industrial Revolution and Healthcare" which is sponsored by the Ministry of Health and WHO to be held on 24th - 26th October 2018 at the Kingsbury Hotel in Colombo.

A very interesting seminar on "Drug Trafficking Trends in the Indian Ocean and the impact on Sri Lanka" by Mr. Shanaka Jayasekera (Programme Co-ordinator) (Indian Ocean Region) Global Maritime Crime Programme (GMCP) of the United Nations Office on Drugs and Crimes (UNODC) was held on Tuesday 16th October 2018 at the OPA Auditorium in collaboration with the British Scholars Association of Sri Lanka.

EPIDEMIOLOGY AND DETERMINANTS OF TYPE 2 DIABETES IN SOUTH ASIA

Dr. Ranil Jayawardena

Type 2 diabetes has rapidly developed into a major public health problem in south Asia (defined here as Bangladesh, Bhutan, India, Nepal, Pakistan, and Sri Lanka) in recent decades. During this period, major lifestyle changes associated with economic transition, industrialisation, urbanisation, and globalisation have been key determinants in the increasing burden of non-communicable diseases. A decline in nutrition quality, reduced physical activity, and increased sedentary behaviours are reflected in the increasing prevalence of type 2 diabetes and related risk factors in the region. The International Diabetes Federation 2017 estimates of the prevalence of diabetes in adults in the region range from 4·0% in Nepal to 8·8% in India. The prevalence of overweight ranges from 16·7% in Nepal to 26·1% in Sri Lanka, and the prevalence of obesity ranges from 2·9% in Nepal to 6·8% in Sri Lanka. An increasing proportion of children, adolescents, and women are overweight or obese, leading to a heightened risk of type 2 diabetes. Ethnic south Asians present with greater metabolic risk at lower levels of BMI compared with other ethnic groups (referred to as the south Asian phenotype), with type 2 diabetes often developing at a younger age, and with rapid progression of diabetic complications. Because of the presence of multiple risk factors and a body composition conducive to the development of type 2 diabetes, south Asians should be aggressively targeted for prevention. In this Series paper, we detail trends in the prevalence of diabetes in the region and address major determinants of the disease in the context of nutrition and physical activity transitions and the south Asian phenotype.

Introduction

The development of type 2 diabetes as a major public health problem has been particularly rapid in much of south Asia since the 1990s.[1] In this period, the region has experienced pronounced demographic, epidemio-logical, and socioeconomic changes,[2] with important consequences for population health. Type 2 diabetes results from an interplay between genetics and the environment-in the context of the increasing prevalence in south Asia, environmental factors include a combination of increased energy intake and decreased energy expenditure, plus a genetic susceptibility to such lifestyle changes.[3] South Asian people have several distinct features with respect to type 2 diabetes compared with other ethnic groups, including an earlier onset of disease and complications, occurrence at a lower BMI, and increased β-cell dysfunction, insulin resistance, and ectopic fat deposition.[4] The rapid increase in the prevalence of type 2 diabetes in south Asia underscores the challenge facing policy makers and clinicians with respect to prevention and management. The burden of the diabetes pandemic has important consequences for individuals, families, and communities, and is a major challenge with respect to health-care resources and productivity in the region.

This is the first in a Series of three papers about type 2 diabetes in south Asia. The second paper focuses on clinical management[5] and the third on public health and health systems in the south Asian context.[6] Here, we describe trends in the prevalence of diabetes in south Asia, and address the major determinants of the disease in the context of nutrition and physical activity transitions. We also consider the concurrent influence of overweight and obesity and the south Asian phenotype.

Epidemiology of type 2 diabetes and obesity and its determinants in south Asians

Prevalence and projections

The global diabetes pandemic has been referred to as a "tsunami", with the potential to exert inexorable and unsustainable pressure on health costs.[7] The constellation of prediabetes, metabolic syndrome, and diabetes is a major public health concern and the substantive increase in prevalence in recent decades in south Asia is greater than that seen in high-income regions.8 Notably, about a quarter of the world's population live in the south Asia egion (here defined as Bangladesh, Bhutan, India, Nepal, Pakistan, and Sri Lanka), which helps to indicate the scale of the public health challenge.

It is important to highlight that estimates of diabetes in south Asian countries are often based on data from few studies and dominated by data from India. Even with respect to India, data have been sporadic and not representative of the whole country.[1] This deficiency led to the implementation of the nationally representative, population-based ICMR–INDIAB study.[9] Similarly, previous studies had not captured the heterogeneous nature of diabetes in India. The major aim of the ongoing ICMR–INDIAB study is to estimate the national prevalence of diabetes and prediabetes by state. The most recent iteration of this large cross-sectional study of the prevalence of diabetes (both type 1 and 2) and prediabetes in 15 states of India was reported in 2017.[9] The overall

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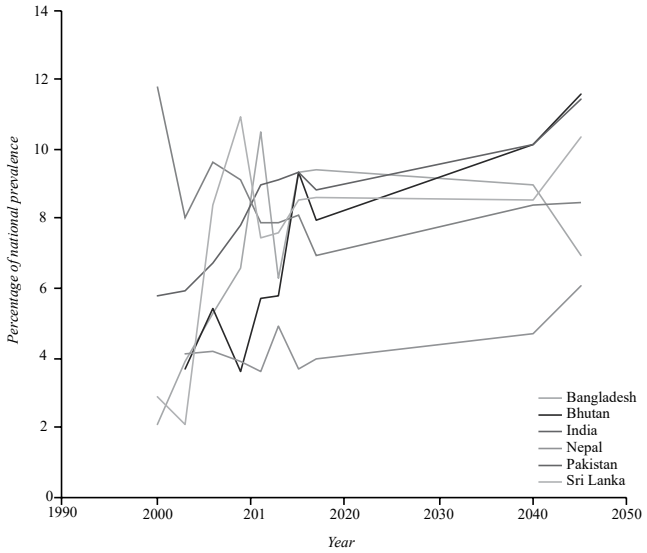

figure shows the secular trends in prevalence of diabetes across the region from 2000, with projections to 2045, based on data from the IDF.[10] The table details the prevalence of diabetes and related risk factors for men and women across the region, based on data from WHO.[11,15] By 2045, an estimated 134 million Indians will have type 2 diabetes, up from a 2017 estimate of about 72 million. Currently, only China exceeds India in the absolute number of cases of diabetes worldwide, with Pakistan and Bangladesh placed 11th and 12th, respectively.[10]

It is important to note that comparisons of diabetes prevalence between countries and world regions can be challenging, particularly as most estimates have

Figure: Secular trends in the prevalence of diabetes in adults (aged 20-79 years) from 2000 to 2017, with a projection to 2045

	Overweight (≥25 kg/m²)			Obesity (≥30 kg/m²)			Type 2 diabetes		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
Bangladesh	14·4%	19·6%	17·0%	2·0%	4·6%	3·4%	8·6%	7·4%	8·0%
Bhutan	23·3%	26·6%	24·8%	4·6%	7·5%	5·9%	9·5%	8·9%	9·2%
India	19·0%	23·9%	21·4%	3·1%	6·5%	4·7%	7·9%	7·5%	7·8%
Nepal	13·6%	19·6%	16·7%	1·7%	4·1%	2·9%	10·5%	7·9%	9·1%
Pakistan	19·1%	22·7%	20·8%	3·3%	6·4%	4·8%	10·0%	9·7%	9·8%
Sri Lanka	18·9%	32·9%	26·1%	3·5%	10·0%	6·8%	7·3%	8·4%	7·9%

Table: Age - standardised prevalence of overweight, obesity, and type 2 diabetes in adults (aged 18 years and older) in south Asia in 2016, by country and sex [11,15]

prevalence of 7·3% was similar to the WHO estimate, but lower than the most recent International Diabetes Federation (IDF) estimate (8·8%).10,11 Notably, the overall prevalence of prediabetes in the ICMR–INDIAB study was 10·3%. Based on data from this and other studies, including the Chennai Urban Rural Epidemiology Study (CURES) of a large representative sample from Chennai, India,[12] and the National Urban Diabetes Survey (NUDS), which was completed in 2000,[13] diabetes prevalence has increased dramatically in urban India. The ICMR–INDIAB data[9] showed a higher prevalence in urban (11·2%) than rural areas (5·2%), and a higher prevalence in low socioeconomic status groups in urban areas within more affluent Indian states. In 2018, Geldsetzer and colleagues[14] reported a crude prevalence of diabetes in India of 7·5%, based on a nationally representative sample of adults. Crude prevalence among states varied from 3·2% to 19·9%.

Despite shortcomings regarding data across the region, projections regarding diabetes are daunting. According to IDF estimates,[10] the prevalence of diabetes in adults (crude percentage) across south Asian countries is similar, with the exception of Nepal (8·8% in India, 8·6% in Sri Lanka, 6·9% in Bangladesh, 7·9% in Bhutan, 6·9% in Pakistan, and 4·0% in Nepal). The

been modelled from poor quality data.[16,17] However, comparisons between south Asia and other global regions can be informative. Globally, an estimated 425 million adults have diabetes and four out of five live in low-income and middle-income countries (LMICs). The southeast Asia (82 million adults) and western Pacific (159 million adults) regions account for a substantial proportion of the total number of adults with diabetes, followed by Europe (58 million), North America and the Caribbean (46 million), the Middle East and North Africa (39 million), South America and Central America (26 million), and Africa (16 million).[10]

It is important to acknowledge that diabetes within and between south Asian countries is heterogeneous, with considerable variability associated with the level of urbanisation, ethnic phenotypes, and socioeconomic status.[9,18] To date, a higher prevalence of diabetes and obesity has been seen in more edu cated, more affluent, and urban south Asians, attributable to transitions in nutrition and lifestyle (physical activity) associated with rapid economic development.[19,20] However, in recent years, evidence has emerged showing an increasing prevalence of diabetes and obesity in middle and low socioeconomic strata and rural settings.[21]

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Adding to the scale of the challenge for the region is the problem of underdiagnosis of diabetes.[22] Notably, almost half (47·3%) of the individuals identified with diabetes in the ICMR–INDIAB study[9] were previously undiagnosed. Further more, with evidence of increases in diabetes prevalence in people of low socioeconomic status, most of whom live in rural areas with poor access to health services, a substantial degree of underdiagnosis in this population is highly likely.[22]

Contribution of nutrition and lifestyle transitions

Worldwide, physical inactivity is estimated to cause 6–10% of cases of coronary heart disease, type 2 diabetes, breast cancer, and colon cancer.[23] Rapid improvements in socioeconomic conditions have contributed to transitions in nutrition[24] and lifestyle in south Asia.[2] For many south Asians, the traditional rural way of life, with its high daily energy expenditure associated with manual labour, has been replaced by a lifestyle of lower energetic demands and increased sedentary behaviours upon transitioning to an urban setting. Increased availability and extensive marketing of low-cost, energy-dense foods, plus globalisation of food production have contributed to the increased prevalence of obesity.[25] Other reasons for the rapid increase in the number of south Asians with type 2 diabetes include increased life expectancy, population growth, and ageing, as well as more proactive screening. Worldwide, the increase in the ageing population will see the number of adults aged 65 years and older double by 2050 to about 2 billion. Some 80% of the increase is projected to occur in LMICs, including those in south Asia.[26]

Many south Asian communities are characterised by a double burden of malnutrition, with undernutrition in infants and children and overnutrition in adults. This double burden can often occur in the same individual-being underweight at birth and subsequently gaining weight rapidly in childhood results in increased risk of type 2 diabetes later in life.[27] In general terms, socioeconomic disparities contribute to a worsening of incidence and outcomes of non-communicable diseases, including type 2 diabetes, often compounded by insuf-ficient uptake of health-promoting behaviours, including among the poorest members of society.

Migration

Coincident with the epidemiological transition in south Asia has been a massive increase in rural-to-urban migration28 and a ten-times increase in the prevalence of diabetes in urban India over the past 40 years.29 Estimates suggest that prevalence among people aged 18–65 years in some urban areas is almost 20%.1 With migration to urban areas, an increased risk of type 2 diabetes, obesity, and cardiovascular disease has been attributed to a combination of increased energy intake, particularly refined carbo-hydrates and saturated fats, and increased sedentary behaviour.[30] In one cross-sectional study in India,[31] the prevalence of diabetes among migrants was 14·3%, similar to the urban-dwelling group (13·5%), and much higher than among their rural counterparts (6·2%). Similarly, the proportion of urban, migrant, and rural men classified as obese (BMI >25 kg/m²) were 41·9%, 37·8%, and 19·0%, respectively.[31] Another study in India showed substantial location differences in cardiometabolic risk factors, with urban poor and urban middle class women having higher rates of diabetes, obesity, hypertension, and hypercholesterolaemia, and higher waist circumference compared with women living in rural areas.[32]

We do not address migration of south Asians to other countries in detail here; however, there is mixed evidence on the effect of migration on risk of diabetes. For example, Zheng and colleagues[33] reported on the challenges of acculturation and its contribution to increased prevalence of diabetes and related com plications, and Patel and colleagues34 reported that Indians who have migrated have poorer metabolic profiles than their counterparts in India. By contrast, Gujral and colleagues[35] reported that Indians living in India have a lower BMI and waist circumference compared with their counterparts living in the USA, but had a higher prevalence of diabetes, even at normal levels of BMI. The investigators concluded that the increased prevalence of diabetes in Indians in India was evident in both sexes, across all age groups, and across all levels of BMI.

Overweight and obesity

Overweight and obesity are major risk factors for the development of type 2 diabetes and the prevalence of the disease increased in tandem with increasing trends for overweight and obesity in recent decades.[2,8,19] Age-standardised prevalences of overweight and obesity in adults (aged 18 years and older) are consistently higher in women than in men in all south Asian countries (table).[36] Among men, the prevalence of overweight ranges from 13·6% in Nepal to 22·3% in Bhutan; for women, it ranges from a low of 19·6% in Bangladesh and Nepal to a high of 32·9% in Sri Lanka. The proportions of obese adults are lower, ranging from 1·7% in Nepalese men to 4·6% in Bhutan; for women, the lowest prevalence is in Nepal (4·1%) and the highest in Sri Lanka (10%).

Lifestyle factors such as poor diet, low levels of physical activity, and increased sedentary behaviours have also contributed to increasing overweight and obesity among children and adolescents in south Asia.[37] Obesity in this age group is associated with a

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range of health complications and an increased risk of premature onset of type 2 diabetes and cardiovascular disease.[38] Accordingly, prevention of childhood obesity is a major opportunity in the primary prevention of non-com-municable diseases.[39]

Prevalence of overweight and obesity in women of reproductive age is increasing worldwide.[40] Data from India's National Family Health Survey (NFHS-3) (2005–06) estimates that 13% of women aged 15-49 years are overweight or obese.[41] Women entering pregnancy with an unhealthy body composition contributes to adverse short-term and long-term health outcomes for both mother and offspring, with maternal obesity asso-ciated with intergenerational cycles of increasing obesity and diabetes.[40]

A rapid increase in the prevalence of overweight and obesity in sub-Saharan Africa is also seen as a major driver of diabetes in the region,[16] as is the case in most countries. However, data are mixed regarding prevalence of overweight and obesity in south Asia and other LMICs, including proportions living in urban versus rural settings. More commonly, reports suggest a higher proportion of overweight and obesity amongst urban dwellers.[42,43]

It is important to note that a positive energy balance (arising from an intake of excess energy, a decrease in energy expenditure, or both) has been linked to an increased exposure to unhealthy, non-traditional foods;[25] however, a surplus of local food above energy needs is also problematic. Importantly, an estimated 30% of Indian patients with type 2 diabetes are non-obese,[44] a paradox we discuss in the context of the south Asian phenotype.

Gestational diabetes

South Asian women living in the region have a higher risk of developing gestational diabetes than do white Europeans.[45] Maternal obesity is strongly associated with gestational diabetes, the prevalence of which is increasing worldwide, including in LMICs. However, it is difficult to ascertain the prevalence in south Asia and some other world regions because of the challenge of obtaining reliable data.[45,46] The authors of a 2015 review[47] estimated that the population attributable risk of gestational diabetes from increased maternal BMI was 50% in India. They posited that elimination of overweight or obesity before or early in pregnancy would greatly reduce gestational diabetes, pre-eclampsia, and pregnancy-induced hypertension. Seshiah and col-leagues48 completed a large community-based study in south India and detected gestational diabetes in 17·8%, 13·8%, and 9·2% of women in urban, semi-urban, and rural areas, respectively; however, this study is over 10 years old and the levels of gestational diabetes might have increased substantially in this period. An estimate from 2012 suggested a prevalence of gestational diabetes in Bhawalpur, Pakistan, of 14·5%.[49]

South Asian phenotype and type 2 diabetes

Key features

A south Asian or Indian phenotype with high body fat, often within a normal bodyweight and BMI category, but with a heightened risk of type 2 diabetes, has been widely referenced.[25,44,50] In some parts of the region, stunting is an acknowledged component of this phenotype and indicative of intergenerational undernutrition. Notably, compared with white European populations, the average height of Indians and other south Asians has not increased much in the past 150 years.[51] Despite no universal definition of the metabolic profile of the phenotype, it is commonly characterised by insulin resistance, hyper glycaemia, low HDL cholesterol, and high triglycerides within a normal bodyweight range.[52]

In addition to the description of Indian babies as thin-fat, a term coined by Yajnik[53] to refer to the unique characteristics of the south Asian phenotype from birth, other descriptive terms such as high fat–low muscle mass,[54] high fat–normal weight–low muscle mass,[55] and metabolically obese–normal weight,[54,55] have been used. Prado and colleagues56 referred to abnormal body composition such as high adiposity or low muscle mass, or a combination of the two-high adiposity-low muscle mass (sarcopenic obesity)-in the context of ageing.[56] Excess adiposity is associated with an increased risk of a range of disease states, including type 2 diabetes; however, the high fat-low muscle phenotype has not been systematically explored across the lifespan, nor across the BMI spectrum.[56] A better understanding of the contri bution of compartments of body composition to health is important across the lifespan, with objective measurement of composition more relevant than the commonly used epidemiological measures and indices, including BMI, waist circumference, and skinfold thickness.

Body fat differences

A high percentage of body fat and a predominance of abdominal fat are particularly common in many south Asians. Diabetes is diagnosed in south Asians at a younger age and with a thinner physique compared with white Europeans.[51,57-60] A study in newly diagnosed Indian patients with type 2 diabetes and controls without diabetes showed that central obesity (as measured by waist-to-hip ratio) had a stronger association with glycaemia than did BMI.[61] Despite their lower BMI compared with white Europeans, the south Asian phenotype is typified by a higher waistto-hip ratio, higher subscapular skinfold thickness, higher

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body fat (adiposity), and higher abdominal fat (both subcutaneous and intraabdominal visceral).[44,55] Several factors, including the potential role of adipocyte anatomy (adipocytes are larger in south Asians[44,55]), and heightened adipocyte inflam matory response,[44,55] remain to be systematically researched.

Another factor likely to exaggerate the south Asian phenotype, as well as affecting some populations in other regions, is rapid or excessive postnatal growth. This growth could be a consequence of poor growth in utero (catchup to achieve genetic potential) or the result of excess feeding. Excess feeding might be partly driven by health professionals and associated with a rapid nutrition transition. In a longitudinal study of children in Pune, India, those who were born small but grew large as 8yearold children had the highest adiposity, were centrally obese, insulin resistant, had the highest cholesterol concentrations and blood pressure-ie, the most adverse cardiovascular risk profile.[62] Similarly, data from the earlier New Delhi Birth Cohort showed that those who were hyperglycaemic at age 28 years were born with a low birthweight, had poor growth in the first 2 years of life, but had rapid growth in childhood and adolescence.[63] The occurrence of such events during reproductive age might have deleterious effects on the next generation through intrauterine and postnatal programming.[51,64]

Studies highlighting the implications of nutritional deficiencies and as yet unknown factors during intra-uterine, neonatal, and early childhood periods provide interesting links to type 2 diabetes and hypertension in adults. Given the long timelines of development of disease, these issues are not easy to explore in shortterm studies. It is possible that predisposition to these diseases could be reduced if proper nutrition, an appropriate body composition, and adequate physical activity were achieved from early life.[65,66]

Small, short, and thin Indian newborn babies (eg, 2·7 kg, 47·3 cm, 24·6 kg/m²) have been reported to have comparable subscapular skinfold thickness to English neonates (eg, 3·5 kg, 51·1 cm, 27·3 kg/m²),[67] but higher superficial and deep subcutaneous and visceral abdominal fat,68 and lower lean body mass.[69] The thin–fat phenotype seen in south Asian babies is biochemically characterised by higher leptin and insulin and lower adiponectin concentrations in the cord blood than in white neonates, features that persist into later life.[53]

Importantly, abdominal body fat (subcutaneous and intraabdominal visceral),[58,59] and, in particular, ectopic fat in the liver and pancreas, could contribute to diabetes in south Asians.[70] Furthermore, the subcutaneous layer of abdominal adipose tissue is thicker in south Asians and is associated with metabolic syndrome, independent of intraabdominal and total body fat.[71] In addition to higher adiposity, many south Asians have reduced skeletal muscle mass and organ size compared with white Europeans.[72] The reduced metabolic capacity of south Asians is posited to stem from their low birthweight, which in turn is associated with short stature and low lean mass in adulthood.[51] There is also evidence of ethnic variability in body proportions and increasing evidence that the sarcopenic obesity contributing to the south Asian phenotype might be related to increased propensity for cardiometabolic dysregulation and arterial stiffness.[70,73] Notably, reduced growth and thin physique in south Asians increases susceptibility to central obesity and consequent negative metabolic effects from a combination of diet with a high glycaemic load and sedentary behaviour.[51]

Collectively, despite lower BMI compared with white Europeans, south Asians with type 2 diabetes have higher waisttohip ratio, higher subscapular skinfold thickness, higher body fat percentage, higher abdominal and ectopic fat, lower lean mass, and are likely to have less brown adipose tissue.[58-60] On the basis of these ethnic differences, Indian,[74] Sri Lankan, and now UK NICE guidelines[75] have recommended using lower BMI and waist circumference cutoff values for the diagnosis and treatment of obesity, abdominal obesity, and metabolic syndrome in south Asians. Recommended BMI categories for Asian populations are as follows: less than 18·0 kg/m² for underweight, 18·0-22·9 kg/m² for normal weight, 23-24·9 kg/m² for overweight, and 25·0 kg/m² or higher for obesity. For public health action regarding body fat and diabetes risk, an expert consultation by WHO in 2004 recommended that patients in the BMI range 23-27·5 kg/m² be considered at an increased risk for type 2 diabetes and cardiovascular disease, and those in the range 27·5 kg/m² or above be considered as high risk. Despite these alternative cutoff points, the variability in diabetes both within and between south Asian countries and other regions cannot be fully explained solely by differences in BMI.[51] Accordingly, we summarise a range of contributing factors associated with predisposition to type 2 diabetes, including the south Asian phenotype, in the panel.

Drivers of type 2 diabetes in south Asia

Genetic factors

Type 2 diabetes and its progression are characterised by a complex interplay between genetics and the environment. There are substantial ethnic differences in the underlying genetic architecture of the disease,[76] with south Asians having a higher risk of diabetes than white Europeans.[2]

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More than 80 loci associated with susceptibility to type 2 diabetes have been identified, but account for less than an estimated 10% of the genetic component of the disease.[77] Despite similar genetic markers of diabetes and obesity in south Asians and other populations, genotype–phenotype associations for both conditions with respect to the FTO gene are different in south Asians to those in white Europeans.[78,79] Sharma and colleagues80 attempted to replicate the association of newly identified variants of TMEM163 (transmembrane protein 163) and COBLL1 (cordon-bleu proteinlike 1) with type 2 diabetes in a population in northwest India, but reported a lack of association. The investigators indicated this finding could be because of the heterogeneous nature of the pop ulation, representing multiple ethnic groups. Interest ingly, Bhatt and colleagues[81] showed an association of polymorphisms of the myostatin gene with increased adiposity and low lean body mass in south Asians. Such findings might have implications for the development of insulin resistance and diabetes in the south Asian phenotype, but need further investigation, especially since sarcopenia is a feature of the phenotype.

Importantly, despite the likelihood that genetic factors play a role in predisposing south Asian people to type 2 diabetes, the rapid increase in prevalence of the condition in a relatively short timeframe suggests that environmental factors have a much greater role.[4]

Epigenetics and intrauterine and early life factors

Epigenetics can be defined as the study of changes in gene function that are heritable and do not involve a change in DNA sequence.[82] Epigenetic modifications include DNA methylation and histone modifications. The potential for a strong epigenetic contribution to type 2 diabetes is underscored by the fact that the disease only has a weak genetic component compared with other common traits.[3] Bernstein and colleagues[3] have suggested that environmental factors such as chemical exposures, diet, physical activity, and age might influence epigenetic changes across the life course and affect gene expression and susceptibility to diabetes. Notably intrauterine undernutrition and overnutrition both increase the risk of future diabetes, and have been shown to cause epigenetic modifications to the fetal genome.[83]

It is possible that the south Asian phenotype is epi genetically programmed by maternal nutrition, metabolism, and other unknown factors.84 Maternal nutritional contributors might include vitamin B12 deficiency, B12folate imbalance (low B12 and high folate), and the attendant hyperhomocysteinaemia in the mother,85 but the role of these possible factors require further research. The south Asian phenotype has been observed in studies of firstgeneration and multigenerational migrant Indian adults.[69,72,86,87] New born babies of other ethnic groups in south Asia also have a similar body phenotype.[88] Interestingly, babies born to African mothers in Norway showed a similar phenotype compared with Norwegian white babies.88 Hence, multigenerational undernutrition rather than genetic factors related to ethnicity could play an im portant part in the disease aetiopathology.[88]

Evidence that the high body fat south Asian phenotype exists from birth[53] reinforces the importance of emphasising preconception and maternal nutrition during pregnancy in low socioeconomic groups with increased susceptibility to type 2 diabets in the region.[89] A range of areas require further research, including the role of perinatal nutrition, genetics, and nutrition during childhood.[70,81]

Environmental and lifestyle factors

In addition to obesity, sedentary lifestyle, poor diet, and smoking, factors in the physical environment contribute to the pathogenesis of type 2 diabetes. However, the role of these factors, which include air and water pollution, sleep disruptions, noise from road traffic, and exposure to endocrinedisrupting chemicals, is poorly understood.[90.91,92] As dia betes is a risk factor for both vascular and respiratory disease, research has explored the association between these outcomes in people with diabetes and air pollution exposure;[93] however, the mechanisms are poorly under stood.[91] Findings from systematic reviews and metaanalyses[94] have suggested an association between air pollutants and increased risk for type 2 diabetes, and the investigators of a metaanalysis of cohort studies[95] reported that longterm exposure to fine particulate matter could contribute to the development of diabetes.

In another systematic review and metaanalysis, Eze and colleagues[96] reported a positive association between air pollution and diabetes risk; however, all studies were undertaken in Europe and North America. The substantially greater air pollution (both indoor and outdoor) encountered in many parts of south Asia compared with these western locations suggests that extended exposure to air pollutants might be an important determinant of cardiometabolic health in the region and in other poorer countries, but more research is needed to assess this possibility.[91] The same might be true for exposure to other potential endocrinedisrupting chemicals, including pesticides and industrial solvents, as it is likely that the use of chemical pollutants is more widespread and subject to less regulation in south Asia than in more developed countries. This difference might have a role in the increasing incidence of type 2 diabetes in south Asia.[90]

To be Continued in the October 2018 Newsletter

PUBLISHED BY
INDEPENDENT MEDICAL PRACTITIONERS ASSOCIATION
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