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Review Article

Primary prevention of Type 2 diabetes in South Asians — challenges and the way forward

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Abstract

Preventing diabetes is of enormous value, particularly for the South Asian countries, which have a huge healthcare burden from the onslaught of the disease. Type 2 diabetes has been proved to be preventable using lifestyle changes, even in South Asians despite their heightened risk profile. Strategies to improve awareness about diabetes and translation of preventive measures by innovative, culturally specific programmes have to be implemented at national levels. Integrated involvement of the government, community, media, healthcare and education services, and financial support from national and international organizations, are required. South Asian countries have initiated national programmes for diabetes prevention and management. It is also encouraging to note that joint ventures between developed countries such as the USA, UK and other European countries and centres of excellence in South Asia have been initiated to develop large-scale, community-oriented, pragmatic intervention strategies.

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Introduction

The prevalence of Type 2 diabetes is rising globally. A recent report on the global scenario shows that, of a total of 366 million persons with diabetes, nearly 80% live in the developing countries [1].

South Asian countries, or countries of the Indian subcontinent, constituting India, Pakistan, Bangladesh, Sri Lanka and Nepal, have emerged as the hot spots for the epidemic of diabetes, within a short span of two to three decades. National prevalence of diabetes in adults of 20–79 years are: Bangladesh 9.85%, India 8.31%, Nepal 3.03%, Pakistan 6.72% and Sri Lanka 7.77% [1]. Rapid urbanization, industrialization and modernization have resulted in social and economic uplift, but unfortunately this also has produced adverse health outcomes such as rising rates of diabetes and other metabolic diseases. South Asian populations living in their native lands or in affluent foreign countries have a high prevalence of diabetes [2–5]. It is now evident that 'internal migration' from rural to urban areas within a country unmasks the predisposition for Type 2 diabetes, to the same extent as in South Asian migrants in affluent countries [2,3].

Since 1980, rising trends in prevalence of diabetes and in prediabetic dysglycaemia were observed in the South Asian region and also in many other neighbouring Asian countries [2,3]. China, which had the lowest rates of diabetes until the turn of the century, witnessed an unbelievable leap in the national prevalence, from 6.1% in 2002 [6] to 9.3% in 2010 [1].

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Literature search strategy

Peer-reviewed original research papers and review articles on 'Diabetes in South Asians', 'Diabetes Prevention in South Asians' and 'Genetics/Epigenetics of Type 2 Diabetes' in English were collected by PubMed and Google search. Seminars, textbooks, chapters, publications by the World Health Organization, the International Diabetes Federation (IDF) and the American Diabetes Association (ADA) were referred. Original papers published on prevention of Type 2 diabetes in the authors' literature collection were also used.

Risk factors

Specific characteristics in South Asians

The risk factors of Type 2 diabetes are common in any part of the world, but racial and geographical differences are apparent in their intensity and in the age at manifestation. South Asians have strong racial and genetic predisposition and a strong vulnerability to develop these diseases. In addition, the susceptibility and genetic predisposition to environmental triggers, such as weight gain, unhealthy diet and sedentary behaviour,

predisposes them to develop diabetes at a much younger age than in Western populations [3–5].

Genetic factors

Genome-wide association studies have shown that at least 40 genetic loci are associated with Type 2 diabetes, but these loci confer only a modest effect and do not add to the risk prediction of clinical diabetes beyond the traditional environmental risk factors [7]. Although many of these genes discovered in Caucasians have been replicated in Asians, intra-ethnic differences in the location and frequency of the risk alleles exist. However, the combined effects of multiple genetic variants using genetic scores based on the number of risk alleles appear to be similar in different ethnic groups.

Epigenetic effects

Epigenetic effects are defined as heritable changes to DNA structure that do not involve changes to the DNA sequence. Methylation status of gene promoters *in utero* affects related phenotypes later in a child's development. Epigenetic changes occurring during gestation, possibly maternal nutrition-mediated, appear to influence adiposity and related metabolic phenotypes [8]. Clinically, the findings have the potential to reinforce the importance of adequate nutrition counselling during pregnancy.

The thrifty phenotype or fetal origin hypothesis ascribes the epidemic to malnutrition *in utero*. The 'thrifty genes' existing in South Asians make them susceptible to Type 2 diabetes when affluence becomes common. Therefore, a combination of factors—genetic, intrauterine, accelerated childhood growth and unhealthy lifestyle—increase the predisposition for Type 2 diabetes in the South Asian population [7].

Environmental factors

The rapid increase in prevalence of diabetes in South Asians in the last three decades occurred as a consequence of changes in the environmental factors and not to changes in genetic factors. In these countries, major socio-economic transitions are occurring—malnutrition and under nutrition coexist with over nutrition.

The traditional lifestyle of South Asians, characterized by a diet consisting of complex carbohydrates, low saturated fat and a good amount of physical activity, has been protective against cardiovascular disease and diabetes, even in the presence of enhanced genetic predisposition. Overweight and obesity are increasing rapidly in Asia with the global shift in diet towards energy-dense foods and sedentary lifestyle. These changes, originally observed in Asian immigrants in affluent countries, are now manifested even within the native lands [2–4,7].

Figure 1 is an illustration of the possible interaction of modifiable and non-modifiable risk factors for Type 2 diabetes that promotes the pathophysiological changes. The impacts of primary prevention strategies on reversing or arresting the deterioration are also shown.

Insulin resistance and anthropometric characteristics

South Asians have higher insulin resistance than many other populations [2,3,9,10]. Ethnic differences in features of insulin resistance in the South Asians could be attributed to the peculiarities in body fat distribution, such as higher percentages of visceral fat, truncal fat and dysfunctional large subcutaneous adipocytes [9–11].

Prevention of Type 2 diabetes in South Asia

Primary prevention is of paramount importance to curb the epidemic of the disease. Moving from the 'prevalence–incidence' studies, a paradigm shift is now occurring, with a main focus on primary prevention of Type 2 diabetes.

Several landmark studies in varied racial and geographical areas have proved that Type 2 diabetes is a preventable disease [13–17]. Prevention strategies that improve insulin action and preserve β-cell function can reduce the deterioration of pre-diabetic stages to diabetes [18–20] (Fig. 1).

Despite the adverse profile of the risk factors in South Asians, prospective randomized prevention studies have shown that lifestyle modification and use of metformin can reduce the rate of conversion of pre-diabetes to diabetes [14,16,17]. It is noteworthy that the beneficial changes of preventive strategies in Asian Indians [16] and in Chinese [13] occurred without significant weight reduction, in contrast to the Diabetes Prevention Program (DPP) [14] and the Finnish study [15], in which the benefits were primarily related to weight reduction. Table 1 shows the major studies in Asian populations which demonstrated effectiveness of lifestyle modification in preventing Type 2 diabetes in subjects with impaired glucose tolerance [13,14,16,21,22]. Lifestyle modification is effective in all geographical and ethnic populations of all ages, has collateral benefits on cardiovascular risk factors and is cost-effective [23].

Preventive strategies

The 'Life Circle' approach focusing on modifiable risk factors associated with behaviour and the environment is advisable [24]. Table 2 shows the risk factors in different stages of the life circle and the strategies that should be implemented to prevent diabetes.

Preventive strategies instituted in potential mothers in the pre-conception stage, ensuring adequate nutrition, avoidance of pregnancy in teens or a late pregnancy, appropriate screening for diabetes, infections/inflammation and adequate micro- and macronutrient supply during pregnancy, are steps to reduce the risk of *in utero* malnutrition and its ill effects [24,25]. Good nutrition during infancy and childhood and adequate physical activity among children are important for

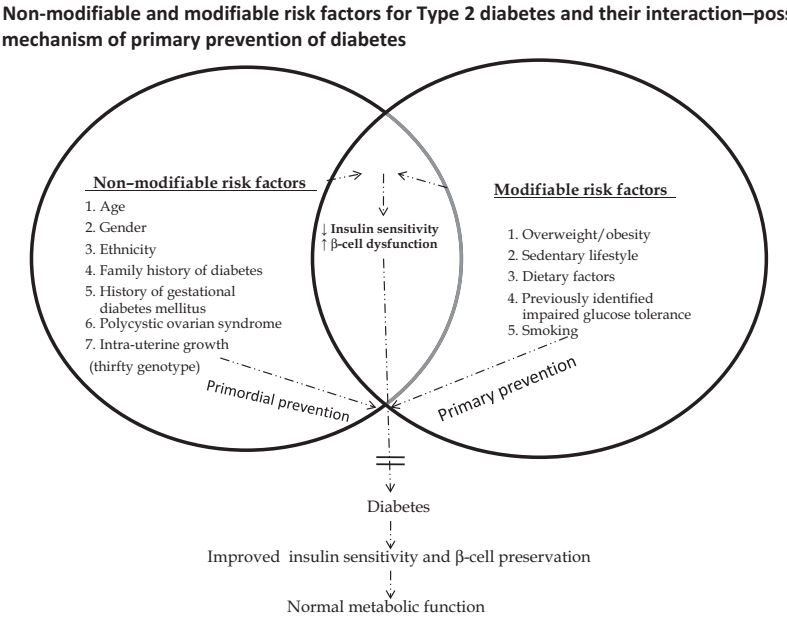

FIGURE 1 Major non-modifiable and modifiable risk factors for Type 2 diabetes are shown. An interaction of these risk factors occurs over a period of time, which worsens both insulin insensitivity and β-cell dysfunction. If intervention by prevention strategies including primordial and/or primary prevention strategies such as lifestyle modification are instituted early, the decompensated stage of clinical diabetes can be prevented. These strategies are shown to improve insulin sensitivity and preserve β-cell function.

the development of a healthy child and an adult. Physical activity, healthy diet, stress-free environment are congenial to healthy life and these habits need to be cultivated and practised during the 'Life Circle'.

Primordial prevention strategies are hard to be implemented. No data are yet available on the feasibility and practically of any strategy, as the results will be apparent only decades later.

Metabolic abnormalities in youth

In South Asians, insulin resistance and other cardiometabolic abnormalities develop in childhood itself [26–30]. South Asian children have higher prevalence of Type 2 diabetes and cardiometabolic risk factors when compared with European children of similar anthropometric characteristics [30]. Strategies to prevent obesity and diabetes in children should focus on family-based interventions, as the families of children with Type 2 diabetes share many anthropometrical and lifestyle risk factors.

Screening for high-risk groups

Several diabetes risk scores using non-invasive risk factors have been published and ethnicity is included in countries with a large percentage of migrant populations [31,32]. Risk score assessment is cost-effective by reducing the number to be screened for primary prevention trials. The benefits of screening would be high among the South Asians, who have a high prevalence of undiagnosed Type 2 diabetes, pre-diabetes and cardiovascular risk factors.

Prevention studies in South Asia

The Indian Diabetes Prevention Programme-1 (IDPP-1) [16] and -2 [17] showed the effectiveness of lifestyle modification in preventing Type 2 diabetes in Asian Indians with pre-diabetes. A small dose of metformin was also effective, but a combination of lifestyle modification and metformin [16] or lifestyle modification and pioglitazone [17] had no additional benefits.

Challenges

Translating research findings into community-oriented upstream programmes poses a huge challenge because of the following characteristics [2,3,27,29].

1. South Asia is a diverse region, with a huge population consisting of nearly 20% of the world's population.
2. Existence of varied rates of literacy, poverty, socio-economic disparities, urban–rural and cultural differences.
3. High risk for Type 2 diabetes, cardiovascular disease, hypertension and associated metabolic disorders.
4. Metabolic abnormalities develop at a young age therefore preventive strategies have to be started in early life.

Barriers

Multiple barriers exist in implementing primary prevention of diabetes in South Asians [29,33,34].

Table 1 Major prevention studies in Asian Populations using lifestyle intervention

Study*	Study population characteristics	Number of patients by treatment group	Duration (years)	Lifestyle goals	Diabetes cumulative incidence	Relative risk reduction (%)
Da Qing Study (1997) Da Qing study (extended) [13]	Chinese Mean BMI: 26 kg/m^2 Mean age: 45 years	*n* = 577 *n* = 568 (by interview medical records)	Mean, 6 years Mean,14 years (total duration 20 years)	Weight loss and maintenance of healthy diet and/or exercise	Control: 67.7 Diet: 43.8 Exercise: 41.1 Diet + exercise: 46 20 years cumulative incidence: 80% intervention, 93% control	Diet: 31 Exercise: 46 Diet + exercise: 42.0 43.0
Diabetes Prevention Program (DPP) Research Group (2002) [14]	Multi-ethnic: 3234 Asian American: 142 Mean BMI Asian American: 28.3 kg/m^2 Mean age: 50.6 years	Control: 1082 Intervention: 1079	Median, 2.8	7% weight loss + 150 min of exercise per week	Control: 11 Intervention: 4.8 (effective in Asian American)	54.0
Diabetes Prevention Program Outcomes Study (DPPOS) (extended) [21]	Multi-ethnic: 2766 Asian American: 124	Lifestyle (*n* = 910) from original lifestyle modification and 932 from original placebo	Median, 7.0 (total 10)	Calorie restriction and weight management	Intervention: 5.9	34.0
Indian Diabetes Prevention Programme-1 (IDPP-1) (2006) [16]	Asian Indian Mean BMI: 25.8 kg/m^2 Mean age: 45.9 years	Control: 136 Intervention: 133	Median, 2.6	Weight maintenance by restricting refined carbohydrates and fat + 30 min of exercise	Control: 55 Intervention: 39.3	28.5
Japanese Prevention Program (2005)§ [22]	Japanese men Mean BMI: 23.5 kg/m^2 Mean age: 51.5 years	Control: 102 Intervention: 356	Mean, 4.0	Reduction in BMI to ≤ 22 kg/m^2 by 30–40 min of exercise per day	Control: 9.3 Intervention: 3.0	67.4

The Indian Diabetes Prevention Programme-1 (IDPP-1) [16] and the Diabetes Prevention Program (DPP) study [14] have shown that Type 2 diabetes can be prevented in South Asians (mostly Asian Indians). Long-term effectiveness of lifestyle modification was demonstrated by the extended DaQing [13], the Japanese Prevention Program [22] and the Diabetes Prevention Program Outcomes Study (DPPOS) [21].

*All study population had impaired glucose tolerance at the baseline of the study.

§In this study, the oral glucose tolerance test used 100 g glucose and modified criteria for recruitment.

Table 2 Primary prevention of Type 2 diabetes, stages and preventive strategies.

Stages	Target group	Risk factors	Preventive strategies
Primordial stage Pre-conception Pregnancy Post-natal follow-up	Potential mother/young females Potential mother/young females Lactating women	Maternal calorie/protein insufficiency. Placental insufficiency Motherhood between ages 13 and 17 years and late pregnancy Known diabetes/previous gestational diabetes Exposure to maternal stress Suboptimal environment of inadequate nutrition Exposure to chronic hyperglycaemia/gestational diabetes leads to permanent diabetes in later life Overfeeding or very low calorie consumption	Adequate micro-/macronutrient supply Increased physical activity Psychological stress reduction Weight management Diabetes management Adequate micro-/macronutrient supply (especially folate and ascorbic acid) Improvement in physical, mental health of mother Weight management Adequate micro-/macronutrient supply Increased physical activity, regular glycaemic monitoring
Infancy/childhood	Infants/children	Low birthweight Accelerated weight gain during infancy and in early childhood Increased consumption of *trans*-fat-containing food Physical inactivity Psychological stress	Breastfeeding during first 6 months and up to 2 years Good obstetric facilities, proper hygiene and medical care to children Removal of soft drinks and junk food from the school environment Promoting physical education and sports recreational activities in schools
Adult	Overweight/obese subjects Subjects with impaired glucose tolerance/gestational diabetes	Physical inactivity Increased consumption of calorie-rich food Psychological stress Sleep disorders Increasing age, first-degree family history of diabetes	Lifestyle modification or use of pharmacological agents such as biguanides or thiazolidinediones

The stages in the 'Life Circle' where risk factors for Type 2 diabetes can develop are shown. The target group, which will be exposed to the risk factors, is identified; possible preventive measures at each stage are also mentioned. Adapted from The Katmandu Declaration (2010) [24], with permission from Elsevier.

Societal barriers

In urban areas, barriers are related to lifestyle changes, sedentary behaviour and escalating levels of mental stress. In rural areas, the barreirs are high rates of illiteracy, poverty, differences in cultural and religious customs, superstitions and misconceptions regarding health management. These barriers exist even in the migrants and native urban populations, depending on educational and social status [32,33,35].

Health system

In these countries, primary health care is mostly devoted to care of acute illnesses and therefore physicians are seldom trained for chronic disease management. Limited availability of trained personnel and lack of a team approach also pose hurdles. In rural areas, physical access to medical services is poor. Moreover, alternative systems of medicine are available and patients frequently change from one treatment to another.

Patient related

The hesitancy to get screened for metabolic diseases such as diabetes result from lack of awareness about its chronic nature, its causes, treatment and complications [33]. Even in affluent countries such as the UK [34], the USA and Canada [35], South Asians are reported to be hesitant to have early screening for diabetes, due to lack of motivation, fear and confusion regarding its benefits and lack of family and social support. The most challenging aspect is the need to practise lifelong behavioural changes. Constant motivation, education and social support have to be provided in order to have widespread, sustained impact at the societal level.

Way forward

Implementation of prevention on a national scale in South Asian countries is definitely an uphill task because of a multitude of barriers, but inaction to face the challenges would be hazardous. Prevention propgrammes at national levels require a multifaceted approach and the following are integral steps for the same [23,36,37]

1. Education of national and local policymakers on the gravity of the problem of diabetes, on the inadequacies in healthcare resources and on the possibility of primary prevention of diabetes.
2. Collaboration of ministries of health, education, information and agriculture to create awareness, and to facilitate healthy lifestyle among members of the public.
3. Evolve cheap and far-reaching strategies to educate, train and motivate the public regarding diabetes.
4. Creation of facilities such as public spaces for walking and other modes of physical activity with better urban development programmes.
5. Implement education on healthy lifestyle from the elementary school level and provide facilities for physical education programmes.
6. Enhance the national capacity for detection, management and prevention of diabetes and other non-communicable diseases by training physicians and paramedical personnel.

Successes

Research endeavours within South Asian countries [16], and in countries where large number of the migrants live [14], have successfully demonstrated the feasibility of primary prevention of Type 2 diabetes in South Asians, despite the propensity of risk factors.

Over recent years, considerable public awareness on non-communicable diseases has been created in many developing countries by international organizations such as the World Health Organization (WHO), International Diabetes Federation, American Diabetes Association, World Bank and World Diabetes Foundation (WDF). Liaison of local organizations with these international organizations has been instrumental in establishing national diabetes control programmes.

National diabetes programmes have been initiated in Bangladesh [38], India [39], Pakistan (40) and Sri Lanka [41]. Nepal is developing strategies to implement similar national programmes [42].

India

Guidelines have been laid down by the Indian Council of Medical Research (ICMR), Government of India, for providing minimum standards of care, prevention, survey of disease prevalence and training health resource personnel [43]. The Ministry of Health and Family Welfare has launched the pilot phase of the National Programme for Prevention and Control of Diabetes, Cardiovascular Diseases and Stroke (NPDCS) [39]. Its objectives are: (1) health promotion for the general population by creating awareness on lifestyle-related diseases, with focus on adopting healthy lifestyles in schools, the community and places of work; and (2) disease prevention for those at high risk through screening and targeted intervention to reduce mortality and morbidity as a result of non-communicable diseases.

A cascading effect is anticipated by creating a cadre of trainers who are able to train large numbers of local physicians and paramedical personnel, using cultural and linguistic approaches. The India Diabetes Research Centre, Chennai, working as a nodal centre, has been able to train more than 4000 doctors and 5000 paramedical personnel from semi-urban and rural areas in 11 states in India with financial support from the World Diabetes Foundation. The programme has sensitized many of the participants to implement similar training programmes in local areas.

Pakistan

A 3-year diabetes prevention programme [the Pakistan diabetes prevention programme (PDPP)] was initiated in December 2011, in Karachi (Clincial Trial Registry No; NCT 01530165) by the Aga Khan University in collaboration with the International Diabetes Federation and Helsinki University. A national action plan to prevent and control non-communicable diseases and promote health has been developed [40].

Bangladesh

The Diabetes Prevention Intervention Study (DPIS), a joint programme of the Diabetic Association of Bangladesh (BADAS) and the University of Oslo, Norway, to prevent Type 2 diabetes in subjects with impaired glucose tolerance has recently been completed (funded by the World Diabetes Foundation). The objectives of the project have been to raise public awareness about diabetes, to train doctors to improve national healthcare capacity and to develop a national policy for diabetes prevention, with endorsement by the Ministry of Health. Culturally suitable strategies for creation of awareness have been developed [38].

Sri Lanka

The National Diabetes Centre of Sri Lanka, with the collaboration of the scientists at King's College, London, UK, has reported a high prevalence of risk factors for Type 2 diabetes in youth and adults aged 10–40 years [41]. The study is part of a research programme aimed at creation of awareness and developing methods to prevent diabetes in young Sri Lankans.

Nepal

The Nepal Diabetes Association has been active in diabetes detection and awareness-raising programmes [42]. A number of challenges, including issues related to maternal and fetal nutrition and pregnancy and diabetes, have been identified, which are mostly linked to cultural practices and beliefs.

Translation research

Translating the findings from a clinical research setting to the less-than-optimal real-world environment is a big challenge. The National Institutes of Health (NIH), USA and BRiDGES (Bringing Research in Diabetes to Global Environments and Systems), initiated by the International Diabetes Federation, are promoting translation research projects in diabetes prevention and treatment in developing countries.

The Diabetes Community Lifestyle Improvement Programme (D-CLIP), a collaborative project between the Madras Diabetes Research Foundation (MDRF), Chennai, India, and the Emory University, USA, has been initiated in Chennai, India, which is a culturally specific translation interventional programme sponsored by the BRiDGES (Clinical Trials Registry No; NCT 01283308) [44]. A similar study, South Asian Health and Prevention Education (SHAPE), by the partner in the USA investigates the effectiveness of lifestyle in South Asians living in Atlanta, USA (Clinical Trials Registry No; NCT 01084928) [45].

A prospective study on 'The Role of Information Technology in the Prevention of Type 2 Diabetes' conducted by the India Diabetes Research Foundation (IDRF), Chennai, India, and the Imperial College, London (Clinical Trials Registry No; NCT 00819455), received the UK India Education and Research Initiative (UKIERI) award by the British Council in 2008. The study aims to test whether diabetes prevention can be achieved at lower cost using mobile phones for education, training and motivation. It is also aimed at developing research protocols and a computerized algorithm to test this hypothesis in India for application in UK and, subsequently, elsewhere.

Another similar project is jointly funded by the Indian Council of Medical Research and the Medical Research Council (MRC), UK, in an effort to address the current disease burden in the respective countries. The collaborative research project initiated in December 2011 is being conducted by the IDRF, Chennai, India, the Metabolic Research Unit, Imperial College, London, and the Epidemiological Research Unit, Cambridge, UK (Clinical Trials Registry No; NCT 01570946).

It is hoped that these studies will evolve cost-effective and practical strategies to prevent diabetes in South Asian subjects despite their high genetic predisposition.

In many developing countries, including the South Asian countries, state and national level prevention programmes, with varied objectives such as raising awareness among school children, rural and semi-urban diabetes prevention and control, and training of resource personnel, have been initiated with the support of the World Diabetes Foundation.

School-based and workplace-based programmes have been successful in creating awareness on healthy lifestyle practices among school children, teachers and the families [29,46]. However, children gave low priority for health and were resistant in making lifestyle changes; the staff also faced barriers related to competing priorities and resource limitations [29]. Hence, strategies have to be modified to improve the compliance.

In the UK, many ongoing programmes funded by Diabetes UK, the Welcome Trust, the Medical Research Council, South Asian Health Foundation (SAHF) and National Institute of Health Research (NIHR) are investigating preventive aspects of diabetes using structured education and culturally suitable strategies for South Asian populations [47].

The National Diabetes Education Program (NDEP) in the USA was sponsored by the Department of Health and Human Services, National Institutes of Health and the Centers for Disease Control and Prevention (CDC) [48]. The Asian American Pacific Islander Work Group of the National Diabetes Education Program focuses on education and communication approaches to address diabetes prevention and control. Awareness creation among the population through culturally acceptable methods is shown to be feasible even among the most conservative sections of South Asian immigrants in the UK [49].

Collaborative research and dynamic partnerships between researchers and organizations involved in genetic, epi-genetic and environmental influences on development of Type 2 diabetes are being initiated in search of innovative strategies for primary prevention of diabetes. Such endeavours are supported by the European Union under its 'Specific International Cooperation Action (SICA)' funding scheme [50]. The EPI-MIGRANT (Identification of epigenetic markers underlying increased risk of Type 2 diabetes in South Asians) initiated in December 2011 brings together experts from Australia, Finland, India, Italy, Japan, Mauritius and the UK to evaluate lifestyle, environmental, genetic and epigenetic risk factors involved in the particularly high rates of Type 2 diabetes in South Asian populations.

Another collaborative venture, the GIFTS (Genomic and lifestyle predictors of fetal outcome relevant to diabetes and obesity and their relevance to prevention strategies in South Asian peoples), started in January 2012, will focus on early life predictors in pregnancy and in the first year of life to halt the epidemic of diabetes and obesity in people from South Asia living in Europe and in the South Asian subcontinent. This multidisciplinary approach by scientists from Bangladesh, Germany, Finland, India, Norway, Pakistan, Spain and the UK, with expertise in prevention strategies, genomics, social science and public health, will develop public health policy, provide guidelines and design large-scale pragmatic interventions to prevent complex diseases [50].

Conclusions

The rapidity with which Type 2 diabetes has increased to a pandemic level in South Asian populations has been dramatic. Over the last few decades, researchers have been successful in identifying the risk factors, in unravelling the pathophysiology and have also shown feasibility and practicality of primary prevention of the disease. Achievement of the ultimate goal of reducing the burden of diabetes by its prevention is likely to take many decades, but it is gratifying that global efforts are being promoted to achieve the goal.

Motivation is essential to get activated, and further strengthening and personal involvement are required for sustained action. Therefore, translation research has to focus on this, using culturally acceptable strategies. The long-term benefits will be multiple, including prevention of lifestyle disorders, behavioural modification, economic gains for the country and improved quality of life.

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Competing interests

None declared.

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