

Challenges in prevention and management of diabetes mellitus and metabolic syndrome in India

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Diabetes mellitus and metabolic syndrome have reached global pandemic proportions with India being designated 'diabetes capital' of the world. Epidemiological studies over the last three decades have shown five-fold increase in the prevalence of diabetes in India, while prevalence rates of >30% have been reported recently for metabolic syndrome. Primary prevention studies have shown significant reduction in relative risk of development of diabetes using lifestyle modifications as well as drugs like metformin, acarbose and rosiglitazone among others. Use of such strategies adapted to suit the local culture along with use of traditional approaches like yoga and ayurveda would go a long way in responding to the challenges posed by these chronic disorders to the country.

Keywords: Diabetes mellitus, epidemiology and risk factors, metabolic syndrome, prevention and management.

Introduction

THE last half a century has seen a surge in the worldwide incidence of diabetes mellitus (DM) and cardiovascular diseases (CVDs) reaching pandemic proportions. The epidemic started in the developed nations and is slowly engulfing the developing and underdeveloped world. The opening of the Indian economy has resulted in rapid economic boom and urbanization in this country. However, this prosperity has also brought along with it the silent killers – CVD and diabetes. The rising trend of obesity and insulin resistance, along with a constellation of other abnormalities, together comprising the metabolic syndrome, is a disturbing portent for the future health of the nation. The silver lining is that, recent scientific evidence suggests that it is possible to prevent or delay diabetes and CVD, thus slowing this epidemic. In this article, we discuss the epidemiology and risk factors for metabolic syndrome and DM in India and the challenges in their prevention.

Definitions and pathogenesis

DM is a multi-system disorder comprising metabolic and vascular abnormalities resulting from insulin deficiency, with or without insulin resistance. The disorder is classified into various types and subtypes based on etiology¹. Type 2 DM, the form driving the current epidemic of diabetes, results from a combination of loss of pancreatic beta cells and peripheral tissue resistance to the actions of insulin. Premature and exaggerated loss of beta cells is accounted for genetic factors and metabolic defects like lipotoxicity, glucotoxicity and deposition of amyloid. Insulin resistance results from genetic factors, decreased physical activity, ageing and obesity^{2,3}. This is shown in Figure 1.

Metabolic syndrome refers to a group of metabolic abnormalities that result in increased risk of CVDs. First

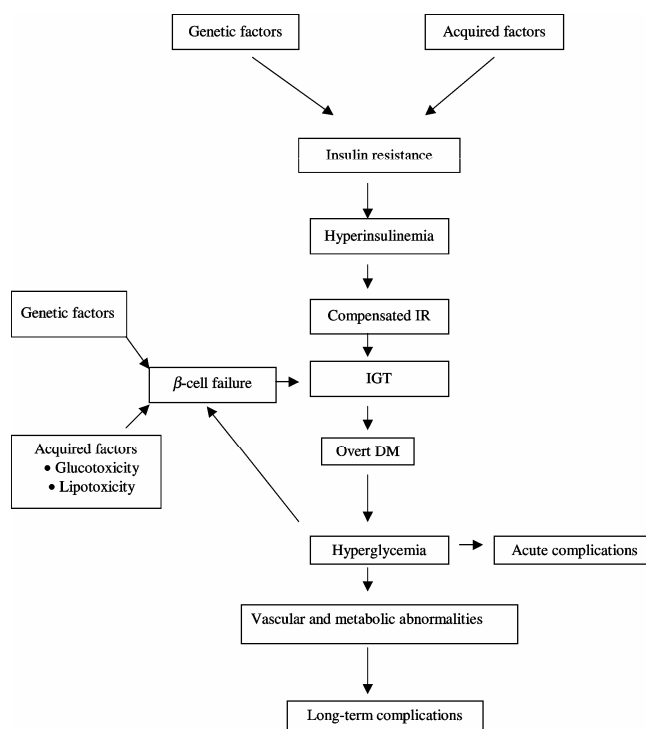


Figure 1. Pathogenesis of type 2 diabetes mellitus. IR, Insulin resistance; IGT, Impaired glucose tolerance; DM, Diabetes mellitus.

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Table 1. Definitions of metabolic syndrome

| Risk factors | NCEP-ATP III definition ⁶ , 2001 | WHO definition ⁷ , 1998 | AACE definition ⁸ , 2003 | IDF definition ⁹ , 2005 |
|--------------------------|--|---|---|---|
| Obesity* | | | | |
| BMI | – | ≥ 30 kg/m ² | ≥25 mg/m ² | – |
| Waist circumference (cm) | | – | – | Ethnic specific South Asians; South, Central Americans |
| Men | >102 | | | ≥90 |
| Women | >88 | | | ≥80 |
| | | | | Europids |
| | | | | Chinese |
| | | | | Japanese |
| Waist-hip ratio | | | | |
| Men | – | >0.9 | – | – |
| Women | – | >0.85 | – | – |
| Triglycerides (mg%) | ≥150 | ≥150 | ≥150 | ≥150 |
| Low HDL (mg%) | | | | |
| Men | <40 | <35 | <40 | <40 |
| Women | <50 | <39 | <50 | <50 |
| Blood pressure (mmHg) | ≥130/85 | ≥140/90 or use of anti HT drugs | ≥ 135/85 | ≥ 130/85 or previously diagnosed HT |
| Glycemia | FPG ≥ 110 mg% | Type 2 DM or IFG or IGT or low glucose uptake (below lowest quartile using hyperinsulinemic euglycemic clamp) | FPG ≥ 110 mg% 2 h post-glucose challenge > 140 mg% | FPG ≥ 100 mg% or previously diagnosed type 2 DM |
| Others | – | Urinary albumin excretion ≥ 20 µg/min or Urinary alb: Cr. ratio ≥ 30 mg/g | Family h/o type 2 DM, HT or CVD PCOS Sedentary lifestyle Advancing age Ethnic group with high risk for type 2 DM or CVD | – |
| Diagnostic criteria | Presence of any three of these five factors defines presence of metabolic syndrome | Presence of insulin resistance plus any two other factors | Clinical judgment for applying definition | Obesity plus any two of the next four |

NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; IDF, International Diabetes Federation; BMI, Body Mass Index; FPG, Fasting Plasma Glucose; IFG, Impaired Fasting Glucose; IGT, Impaired Glucose Tolerance; HT, Hypertension; PCOS, Polycystic ovarian syndrome; CVD, Cardiovascular disease; DM, Diabetes mellitus; alb : Cr ratio, Albumin creatinine ratio.

‘–’ refers to the absence of the risk factor from that definition.

*Different indicators of obesity have been used in different definitions, with some preferring markers of global obesity like BMI, while others have used those of central obesity like waist circumference or waist-hip ratio.

described by Reaven in 1988, it is also called syndrome X or insulin resistance syndrome. It is characterized by obesity (predominantly abdominal), insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, hypertension, hyperuricemia and other markers of pro-inflammatory and pro-thrombotic state^{4,5}. Presently, four different organizations have proposed separate definitions for metabolic syndrome (Table 1). Though each has different criteria and cut-offs, the importance of obesity, hyperglycemia, hypertension, high triglycerides and low HDL is

central to all definitions^{6–9}. Recent scientific evidence suggests that the cut offs should be ethnicity-specific. This is especially true in the case of Asian Indians, who have lower BMI and waist circumference for a similar or higher degree of insulin resistance and CVD risk compared to white Caucasians^{10,11}. This information is reflected in the most recent definitions. The central pathogenic feature is the insulin resistance resulting from genetic factors as well as abdominal obesity. The subsequent hyperinsulinemia results in all other abnormalities

that singly or in combination increase risk for CVD (Figure 2).

Extent of the problem of DM and metabolic syndrome in India

DM has been known in India since ancient times. The Ayurveda describes it under 'Madhumeha', a disease primarily of the affluent and the aged. This had been the trend worldwide also, till a few decades ago. However, the last three decades have seen an alarming rise in global prevalence of type 2 DM. Currently, around 170 million individuals are affected and the numbers are expected¹² to double by 2030. More worrisome is the rising prevalence in children and young adults. India is the unofficial 'diabetes capital of the world' with an estimated 40 million affected and the numbers expected to reach 80 million by 2030. Certain features typical to Indians make them more vulnerable to this disease and at a younger age. The 'Asian Indian phenotype' predisposes to type 2 DM and premature CVD (metabolic syndrome), thereby adversely affecting the nation's health and economy.

Prevalence of Type 2 DM in India

Epidemiological studies to estimate the prevalence of DM have been conducted since 1970s. A list of these is given in Table 2 along with estimated prevalence and other

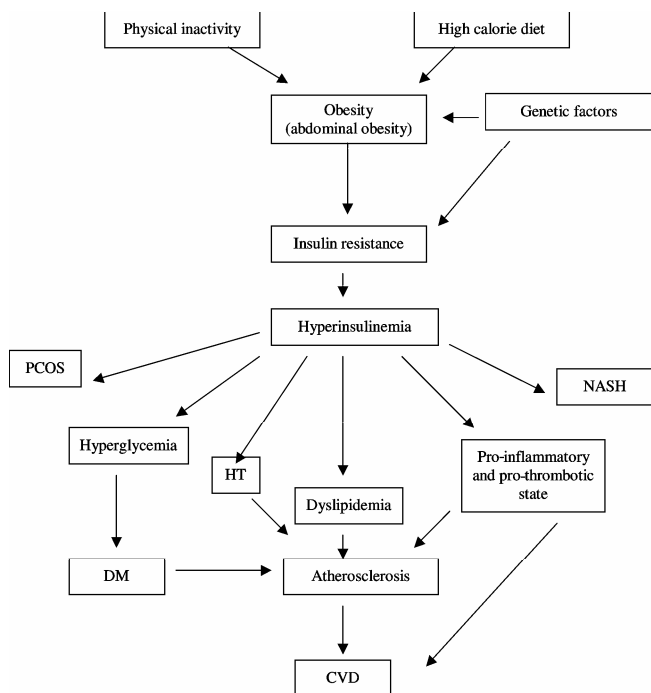


Figure 2. Pathogenesis of metabolic syndrome. PCOS, Polycystic ovarian syndrome; HT, Hypertension; NASH, Non Alcoholic Steatohepatitis; DM, Diabetes mellitus; CVD, Cardiovascular disease.

details. While most studies have been conducted in one state or region, some involved a group of states, thereby estimating national prevalence. Some of the differentiating features of these studies include urban vs rural, North Indian vs South Indian, methodology used to diagnose DM and various age groups included in the study. Some of these studies are described below with the aim to highlight the rising prevalence of DM.

The first national study was conducted in 1972 by ICMR^{13,14}. It involved six states with 30,000 subjects >14 years of age. Capillary glucose >170 mg/dl was used to diagnose DM. The urban prevalence of DM was 2.1% and rural 1.5%, while in those >40 years, it was 5 and 2.8% respectively. Ramachandran *et al.*¹⁵ reported a prevalence of 8.2% in urban and 2.4% in rural areas from a study in Chennai in 1988. Five years later, the same group repeated the study in the same area and reported¹⁶ an urban prevalence of 11.6%. The National Urban Diabetes Survey (NUDS) was conducted in six metros in 2000 and involved more than 10,000 subjects >20 yrs of age. It reported an age-standardized prevalence of 12.1%. Hyderabad had highest prevalence at 16.6% while Mumbai had lowest at 9.3%. Overall the prevalence was higher in South India. Impaired glucose tolerance (IGT) was identified in 14% of the subjects¹⁷. The Chennai Urban Rural Epidemiology Study (CURES)²⁰ conducted on 26,000 subjects in Chennai reported crude prevalence of type 2 DM and IGT to be 15.5 (age standardized 14.3%) and 10.6% respectively. Thus from 1989 to 2004, the prevalence of DM increased in Chennai by 72% (8.3 to 14.3%). The higher prevalence in some of these studies^{17,20} could be attributed to the study population being from metropolitan cities. The Prevalence Of Diabetes in India Study (PODIS)¹⁹ reported a prevalence of 4.7% in urban and 2.0% in rural areas using ADA 1997 criteria. The recent WHO-ICMR national NCD study reports²³ a prevalence of 7.3% in urban and 3.1% in rural areas using a sample size of over 40,000. The relatively lower prevalence in these two studies could be due to differences in the criteria used for diagnosis of diabetes (ADA 1997, self-reported diabetes), sampling areas (rural, peri-urban and urban) and the determinants used for their classification. Further, these studies gave additional insights into the high burden of diabetes. These include:

(1) A high ratio of known : unknown diabetes^{20,24} ranging from 1.5 to 2.0. This underscores the need for identifying individuals through simple screening tools before they develop complications.

(2) The presence of pre-diabetes, a large pool that over a period of time will convert to diabetes. NUDS reported IGT in 14%; a study in Kerala reported²² pre-diabetes in 11.2%, while CURES reported IGT in 10.6%. These individuals have to be identified with the aim to intervene and prevent the progression to DM.

(3) A large urban-rural gradient: A higher prevalence was observed in urban areas compared to rural areas in

Table 2. Studies on the prevalence of DM in India

| Author and year | State/ region | Community | Sample size | Age (yrs) | Criteria for diagnosis | Prevalence of DM | Age standardized prevalence | Age standardized pre-diabetes prevalence |
|---------------------------------|----------------------------|---------------|--------------------|--------------|--------------------------------------|----------------------------|-----------------------------------|---|
| Ahuja, 1972 (ref. 13) | National (ICMR) | Urban + rural | 34,194 | >14 | RBG | 3.6% 2.1% Ur 1.5% Rr | NA | NA |
| Ahuja, 1991 (ref. 14) | National | Urban + rural | 2572 Ur 6149 Rr | >20 | History, 2 h PG | 4.1% Ur 1.96% Rr | NA | 6.3% Ur 0.32% Rr |
| Ramachandran, 2001 (ref. 17) | Six cities (NUDS) | Urban | 11,216 | ≥20 | History FPG, 2 h PG (WHO 1999) | 13.9% | 12.1% | 14% [#] |
| Asha, Bai, 2001 (ref. 18) | Chennai | Urban | 26,066 | >20 | History | 2.9% | 4.9% | NA |
| Sadikot, 2004 (ref. 19) | National (PODIS) | Urban + rural | 41,270 | >25 | FPG (ADA 1997) | 3.4% 4.8% Ur 1.9% Rr | 3.3% 4.6% Ur 1.9% Rr | 3.6%* |
| Mohan, 2006 (ref. 20) | Chennai (CURES) | Urban | 2350 | ≥20 | History, 2 h PG (WHO 1999) | 15.5% | 14.3% | 10.2% [#] |
| Reddy, 2006 (ref. 21) | National | Urban + rural | 10,442 | 20–69 | History, FPG (ADA 1997) | 10.1% | 8.4% | 6.4%* |
| Menon, 2006 (ref. 22) | Kerala (ADEPS) | Urban | 3069 | 18–80 | History FPG, 2 h PG (WHO 1999) | 19.5% | NA | 11.2% |
| Mohan, 2008 (ref. 23) | National (WHO– ICMR) | Urban + rural | 44,523 | 15–64 | History | 4.5% 7.3% Ur 3.1% Rr | NA | NA |

*IFG, [#]IGT, Ur, Urban; Rr, Rural.

most studies. This signifies the importance of certain environmental factors that are protective and others that potentiate this epidemic. Studies in the developed world, on the contrary, show higher prevalence in rural areas²⁵. Therefore, while it may be low in rural areas now, as the epidemic matures it is likely that the rural population will increasingly get affected to alarming proportions.

(4) Rising prevalence in children and young adults. While in the developed countries, DM occurs in those >65 years, in India, the peak prevalence occurs below the age of 50 years. Data from CURES revealed that as many as 6.6% of those between 20 and 30 years already had type 2 diabetes²⁰.

Prevalence of metabolic syndrome

As the criteria for defining metabolic syndrome have been recently laid down, studies of its prevalence in India are few. Earlier studies described one or more components of the syndrome. Prevalence rates have varied (11–41%) depending on the definition and cut-offs used as well as population characteristics^{26–30}. Using NCEP-ATP III criteria, Ramachandran *et al.*²⁷ reported prevalence of 41% in Chennai, while Gupta *et al.*²⁸ reported 31% in Jaipur. Prabhakaran *et al.*²⁹ recently reported prevalence

of 24.6% from Delhi, with threefold higher prevalence in urban compared to rural areas.

Using data from CURES, the prevalence of metabolic syndrome was 23.2%, 18.3% and 25.8% according to WHO, ATP III and IDF definitions respectively³⁰. Misra *et al.*³¹ have reported 28% prevalence of insulin resistance in urban children and young adults.

Risk factors for DM and metabolic syndrome

Genetic and environmental factors have been implicated in this increasing prevalence of both disorders. Since genetic factors are non-modifiable, this article will discuss mainly the environmental factors associated with the two disorders.

Genes in DM and metabolic syndrome

Diabetes is considered a polygenic disorder with contribution of multiple genes involved in insulin secretion, action and glucose metabolism. Various genes implicated in type 2 DM in different races have been studied in Indians. Pro 12 Ala polymorphism of *PPAR gamma* gene is protective against DM in Caucasians, but not South Asians³². The Thr 394 Thr polymorphism of *PGC 1* gene

is associated with type 2 DM and obesity in Indians^{33,34}. These and other genes could be responsible for the rising trend of diabetes in Asian Indians in the presence of urbanization and other environmental factors.

Environmental factors

The striking increase in prevalence of type 2 DM over the last few years points to the role of the environment in the etiology. In the case of coronary heart disease, it has been observed that the epidemic began in the developed world in higher socio-economic groups and then involved the lower socio-economic rural areas and the decline is in the same direction³⁵. The diabetic epidemic is also showing similar trend in the developed and developing world. In India, prevalence studies show that diabetes is more common in urban compared to rural areas¹⁵. Also, it is more common in higher socio-economic group with white-collar jobs and minimal physical activity^{23,36,37}, and with increased consumption of visible fat with a positive family history of diabetes³⁸. Increased consumption of soft drinks has been associated with obesity and type 2 DM³⁹. Physical inactivity has synergistic effect with obesity on risk of DM²³. Thus, urbanization leading to changing lifestyle with increased consumption of calorie-dense food and physical inactivity lead to abdominal and generalized obesity and type 2 DM as well as metabolic syndrome^{28,29}. Besides this, vitamin D deficiency and more recently, environmental pollution in urban areas, have been implicated in the diabetic epidemic^{40,41}. A recent study evaluating the cardiovascular risk profile in Indians showed that prevalence of diabetes was inversely related to education level among women, while metabolic syndrome was high among those with a lower level of education, although not reaching statistical significance levels. In highly urbanized locations, there was an inverse relationship of the prevalence of diabetes with the level of education, while in peri-urban areas the relationship was direct⁴². A list of the risk factors in some of the recent studies from India is provided in Table 3.

Foetal origin of adult disease

The Barker hypothesis postulates the presence of an inverse association between intrauterine and postnatal

growth patterns and development in adult life of chronic disease like CAD, HT, DM and metabolic syndrome⁴⁴. This has been explained on fetal and maternal under nutrition⁴⁵ and foetal genotype⁴⁶. Research looking at this aspect of etiology of insulin resistance and glucose intolerance has also been carried out in India. The Pune study in children 4 and 8 years of age showed that those born lightest but grown to be heaviest are the most insulin-resistant^{47,48}. The study from New Delhi in adults showed similar results with birth weight positively related to adult lean mass and BMI gain in late childhood and adolescence, predicting adult adiposity^{49,50}. Studies from Mysore have shown direct relation between birth weight and ponderal index with adult-life BMI and adiposity⁵¹. This contrast could be explained by the fact that a thin Indian baby is still fat with increased markers of adiposity compared to lean mass⁵².

Impact of DM and metabolic syndrome on life

Compared with non-diabetics, patients with diabetes have increased risk of morbidities involving multiple organ systems. There is 25 times increased risk of renal failure, 20-fold risk of blindness, 40-fold risk of amputation, threefold risk of stroke and fivefold risk of myocardial infarction. Expected lifespan is reduced by an average of 15 years⁵³. In the developed world, diabetes is the leading cause of blindness, end-stage renal disease and amputation. Compounded with the others factors of metabolic syndrome, the risk is increased several fold.

Besides morbidity and mortality, these disorders impact the socio-economic status of individuals as well as the state⁵⁴. The Bangalore Urban District Diabetes Study (BUDS) estimated the annual direct cost for routine care of diabetes in Bangalore city among lower socio-economic patients in 1998 to be about US\$ 191, while cost per hospitalization⁵⁵ was US\$ 208. Similar estimates have also been provided from North India⁵⁶. The Cost Of Diabetes in India (CODI) study⁵⁷ involving upper socio-economic status patients at multiple centres in the country estimated mean total annual cost of diabetic management to be Rs 21,408, with direct annual cost for out-patient diabetes care being Rs 4724. For a developing country like India with only 5% of its GDP being spent on healthcare, diabetes, especially with complications has a major impact on the socio-economic status.

Table 3. Risk factors for diabetes in India

| Study/Author and year | Region | Risk factors |
|--------------------------|-----------------------|---|
| NUDS, 2001 (ref. 17) | National (six cities) | High income, sedentary physical activity, age, BMI, WHR, family history of diabetes |
| PODIS, 2004 (ref. 19) | National | Age, urbanization |
| ADEPS, 2006 (ref. 22) | Kerala | Age, obesity, family history, <i>Acanthosis nigricans</i> |
| CURES, 2007 (ref. 43) | Chennai | Age, abdominal obesity, family history and physical activity |
| Reddy, 2007 (ref. 42) | National | Low education level (women) |
| WHO-ICMR, 2008 (ref. 23) | National | Urban, sedentary activity and abdominal obesity |

Management strategies

Management of diabetes and metabolic syndrome involves primary and secondary prevention strategies. As noted earlier, both these disorders are associated with various risk factors. Such at-risk individuals, with obesity, low physical activity and family history of disease could be advised interventions to prevent occurrence of the disease. Secondary prevention involves patients who already have developed that disease, with the aim of intervention to prevent complications. This usually involves use of drugs and therapies for the specific disorder.

Primary prevention of DM

Primary preventive strategies could involve one of the following approaches – ‘high risk approach’ with intervention targeted to individuals at highest risk of developing the disease; and ‘public health’ or ‘community approach’ attempting to reduce risk factors in the entire society. The former is usually cost-effective with high benefits for motivated individuals, while the latter benefits society at large. The public health approach involves participation of the community from the outset, including their cultures and traditions^{58,59}.

As diabetes is a disorder resulting from changes in lifestyle, most studies on primary prevention have involved modification of the same. A healthy lifestyle with regular

exercise/physical activity and consumption of fibre rich, low-calorie healthy diet has been the primary intervention. Some studies have used drugs that have anti-hyperglycemic actions or those that improve insulin sensitivity. A list of the major studies^{60–68} is given in Table 4. All these studies recruited subjects with pre-diabetes/IGT (high risk for DM) identified based on certain risk factors and oral glucose tolerance test (OGTT). Lifestyle intervention with a combination of regular physical activity and dietary advice showed an impressive reduction in the risk of developing diabetes in all the studies. In addition, agents such as metformin, rosiglitazone, acarbose and orlistat have also been beneficial in preventing or delaying diabetes.

There has been one study done exclusively in Indians. The Indian Diabetes Prevention Programme (IDPP)⁶⁸ randomized 531 overweight subjects with IGT to one of the four groups – control, lifestyle modification (LSM), metformin or combination of lifestyle modification and metformin with primary outcome being new onset DM by WHO criteria. The 3 years cumulative incidences were 55, 39, 40.5 and 39.5% respectively. The relative risk reduction compared to control was 28.5% with LSM, 26.4% with metformin and 28.2% with a combination of lifestyle modification and metformin, indicating no additional benefit of the combination. Thus, there is strong evidence that type 2 DM can be prevented with an intervention as simple as lifestyle modification.

Table 4. Studies of prevention of DM

| Title and year | Ethnicity | No. of subjects | BMI or wt | Intervention | Outcome | Duration (yrs) |
|------------------------------|-------------------------|-----------------|---------------------------|--|--|----------------|
| DaQing, 1997 (ref. 60) | Chinese | 577 | All groups | Diet vs exercise vs combination vs control | 31% RRR with diet 46% with exercise 42% with combination | 6 |
| DPS, 2001 (ref. 61) | Finnish Caucasians | 522 | Overweight | Diet, exercise (LSM) vs control | 58% RRR with LSM | 3.2 |
| US DPP, 2002 (ref. 62) | Caucasians + minorities | 3234 | Overweight | LSM vs Metformin (850 mg BD) vs Troglitazone vs control | 58% RRR with LSM 31% with Metformin | 2.8 |
| STOP–NIDDM, 2003 (ref. 63) | Caucasians | 1429 | Overweight and obese | Acarbose 100 mg TDS vs placebo | 36% RRR with Acarbose | 3.3 |
| XENDOS, 2004 (ref. 64) | Swedish | 3305 | Obese | LSM, Orlistat 120 mg TDS | 37% RRR with Orlistat | 4.4 |
| TRIPOD, 2002 (ref. 65) | Hispanic women | 266 | All groups (mean BMI >30) | Troglitazone 400 mg/day vs placebo | 50% RRR with Troglitazone | 3.5 |
| DREAM, 2006 (refs 66 and 67) | Multi ethnic | 5269 | All groups (mean BMI >30) | Ramipril 15 mg daily vs placebo, Rosiglitazone 8 mg daily, placebo | 55% RRR with Rosiglitazone; no difference with Ramipril | 3 |
| IDPP, 2006 (ref. 68) | Asian Indians | 531 | Overweight | LSM vs Metformin (250 mg BD) vs combination vs control | 28.5% RRR with LSM, 26% with Metformin 28% with combination | 2.5 |

RRR, Relative risk reduction; LSM, Lifestyle modification.

Efficacy and cost-effectiveness

The Diabetes Prevention Program (DPP) showed that one case of new onset DM could be prevented with every seven subjects with IGT treated for 3 years with LSM and for every 14 subjects treated with metformin⁶². In India, the IDPP showed that approximately seven patients of IGT need to be treated with LSM or metformin for 3 years to prevent one new case of DM⁶⁸. Two factors that determine efficacy and cost-effectiveness of preventive strategies are the criteria used to identify the subjects to be enrolled and the structure of the LSM programme. Most of the trials have used adult subjects (30–60 yrs age), overweight or obese with family history of DM and who had IGT/IFG on standard OGTT. The conversion rate in these individuals is higher than other apparently normal subjects. The ADA describes certain risk factors for increased likelihood of type 2 DM. Using family history, age, anthropometry and physical activity, risk scores for increased likelihood of diabetes have been described and validated in Indian subjects⁶⁹.

The other important factor is the actual LSM programme. The LSM programme in the Finnish Diabetes Prevention Study consisted of dietary advice by physician and nutritionist regarding risk factors for DM and the target BMI to be attained. Plan for a diet (with >50% calories from carbohydrates, <10% saturated fat and 20% mono and polyunsaturated fat, cholesterol <300 mg/dl, protein 1 g/kg/day and dietary fibre of 15 g/1000 kcal) was advised. Both theoretical and practical advice was provided verbally and in printed form. Consultations were held seven times in the first year and then every three months. Three-day food record was obtained at each visit and weight checked. The exercise programme consisted of endurance exercise and supervised sessions twice weekly. This was markedly different from standard advice on diet and exercise provided annually to the control group. The DPP lifestyle programme features included individual lifestyle coaches, structured 16-session core curriculum, supervised physical activity sessions, maintenance interventions, and motivational campaigns among others⁷⁰. The cost-effectiveness has been analysed and reported for two trials. The DPP analysis showed that LSM would cost the healthcare system US\$ 15,700/case of DM prevented, while metformin would cost US\$ 31,300/case of DM prevented compared to placebo. From a societal perspective, LSM would cost US\$ 24,400 and metformin US\$ 34,500/case of DM prevented. Thus LSM was more cost-effective than metformin. Considering the enormous costs of DM management, cost per case prevented seems reasonable^{71,72}. However, using a different model for analysis, Eddy *et al.*⁷³ found the LSM programme of DPP to be too expensive. The IDPP analysis⁷⁴ showed that cost-effectiveness to prevent one case of DM with LSM was Rs 47,341, with metformin Rs 49,280 and with combination Rs 61,133.

Implementation of preventive programmes – Community empowerment

As already discussed, the cost of management of diabetes is enormous. This is compounded by the fact that in India, DM affects young adults, who form the working class. With scarce resources, preventive strategies hold the key in the country. The preventive programmes used in trial setting will need to be adapted, contextualized and implemented in the community. This will require approaches specific for certain regions, cultures and communities. Cost will have to be borne in mind. Such adaptation will need creativity in fund raising and cost containment, the features of the programme as well as involvement of the community. Participatory action research is ideal for prevention of DM and metabolic syndrome. It involves active participation of the intervener and those intervened. This ensures cultural relevance of interventions.

There are few reports describing implementation of preventive strategies in communities⁷⁵. In these studies, a target population was involved in the development, implementation and promotion of the interventions. Culturally relevant messages and tools were used, including traditional foods and knowledge incorporating a holistic approach to health. One such example in this country has been the Chennai Urban Population Study⁷⁶. During the initial study in 1998, 479 individuals from one colony were given advice on a programme for prevention of DM based on diet and LSM. Seven years later, when the same colony was again studied, it was found that the proportion of subjects involving in physical activity and exercise had increased. This was despite the decrease in manual labourers. The people had raised funds to build a park within the colony. This was used for leisure time exercise and mental relaxation. This reflects true effectiveness of preventive programmes. Another such report describing participatory action approach has recently been described from an underserved community in Chennai⁷⁷.

Secondary prevention

Secondary prevention involves management of diabetes with the aim to prevent complications. Various studies have shown that tight control of hyperglycemia reduces micro vascular and macro vascular complications⁷⁸. Besides this, control of blood pressure, dyslipidemia and use of anti-thrombotics form the pillars of overall diabetes management. Metabolic syndrome is also managed along similar lines. Control of obesity, dyslipidemia, blood pressure, insulin resistance, dysglycemia, pro-thrombotic and pro-inflammatory state, results in lower cardiovascular events. Besides individual pharmacotherapy, LSM involving healthy diet and increased physical activity remains the core management strategy.

There are recommendations and guidelines for the management of DM and associated co-morbidities⁷⁹. However, even in the United States, the major targets for diabetes management are not met⁸⁰. The DiabCare Asia–India study provided cross-sectional data on the status of diabetes care in urban India in 1998. Among the 2269 patients from 26 tertiary care centres, mean HbA_{1c} was 8.9 ± 2.1 , with 17% having values $>8\%$. The mean frequency of SMBG was 3.1/month, indicating that much needs to be done for diabetes care in India⁸¹. A more recent study⁸² in 819 middle and upper socio-economic adult patients from Delhi showed that only 13% had HbA_{1c} estimation in the past 1 year and only 16.2% had dilated eye examination; 32% had cholesterol examination and 17% were taking aspirin; 42% had HbA_{1c} $>8\%$ and 40% had LDL >130 mg%. Both these studies underlie the fact that in the best of circumstances, diabetes care in India is sub-optimal. Even in affording patients visiting tertiary care centres, the care provided is sub-optimal and treatment targets are not met.

Management strategies unique to this country

There are certain management issues that are unique to India due to its tradition, culture, geography and people at large. These are briefly described below.

Role of Ayurveda and Yoga

Ayurveda, the science of life, originated in India, more than 5000 years ago. It has been traditionally used as a system of medicine to promote health and well-being, and relieve ailments using a holistic approach⁸³. In this country, a proportion of the population follows this system of medicine, either solely or in combination with allopathic medicine. Diabetes management in Ayurveda includes diet, behaviour and herbal modalities. Various herbs have been described with anti-hyperglycemic actions. Some of these like karela, turmeric, spinach, fenugreek seeds among others, can be part of a healthy diet⁸⁴. Yoga describes stretching and other exercises, besides meditation. These could be incorporated into a healthy lifestyle programme. Thus, knowledge and practices from the indigenous systems of medicine, including Ayurveda can be harnessed for devising preventive strategies⁸⁵.

Urban planning

With industrialization, manual work decreases. To maintain physical activity, leisure time activity has to be increased. This needs safe, open spaces with fresh air and recreational facilities. Our cities have to be planned taking this into consideration. The importance of walkable green spaces has been shown in studies from Japan and

Australia^{86,87}. Roads with pedestrian and bicycle paths, along with playgrounds and parks have to be an integral part of a model city.

Maternal and child health

The foetal origin of adult disease concept shows that low birth weight is a predictor of diabetes and metabolic syndrome. The genetic contribution to low birth weight cannot be changed, but maternal under nutrition as a factor can be alleviated. There is also evidence to rising adiposity and overweight in children⁸⁸. This calls for the need to change the school structure to include physical activity to a greater degree. The ‘child-friendly school initiative’ launched by IAP to further this goal is a welcome beginning. Children have to be educated on the importance of healthy lifestyles⁸⁹.

Polypill

Wald and Law⁹⁰ proposed that a combination pill aimed at simultaneous control of four CVD risk factors – LDL cholesterol, BP, homocysteine and platelet function, when used in patients with CVD or anyone >55 years of age would reduce the risk of IHD events by 88% and stroke by 80%. Their ‘Polypill’ would need six drugs – statin, ACE inhibitor, β -blocker, thiazide, folic acid and aspirin. Used in 100 people, around one-third stand to benefit with gain of around 11 years of life free from IHD or stroke. However 8–15% recipients could have adverse effects. The evidence to include folic acid and a thiazide is debatable. The remaining four could form an ideal polypill, but evidence is required⁹¹. A similar polypill has also been proposed for type 2 DM, combining 1 g metformin, 75 mg aspirin, 40 mg generic statin and 10 mg generic ACE inhibitor⁹². Polypill could go a long way in reducing cost, improving compliance and providing a sustained defence against the epidemics of diabetes and metabolic syndrome without taking anything away from diet and LSM.

‘Train the trainer’ and continuing medical education

As described above, despite diabetes being widely prevalent, the overall standard of diabetes care in this country is poor. General practitioners and physicians, to whom the patients first come, should be aware of screening guidelines, so that maximum cases are diagnosed. They should be aware of recent guidelines on treatment as well as management goals. Successive steps, including referrals to endocrinologists and other specialists should be made aware to them. This can be done at various levels. Revamping the medical education to give more emphasis

on diabetes care is the first step. Conduction of CMEs and seminars helps update knowledge. Repeated surveys to assess the standard of care should be undertaken by government agencies. This provides the feedback to decide remedial action.

Conclusions

The modern epidemics of type 2 DM and metabolic syndrome will increase premature death and disability, directly impacting and impeding the economic progress of the country. Control of these will need judicious use of scarce resources through primary and secondary preventive measures. Though the evidence for most of these interventions is clear from research studies, translation of this to community-based intervention is the next challenge for healthcare professionals and public-health experts.

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