Diabetes: Easier to prevent, but difficult to tame

Diabetes is the fastest growing lifestyle disorder among all noncommunicable diseases with 415 million people living with diabetes in 2015, and this is likely to increase to 642 million by 2040.[1] As projected, India had a dubious distinction of “Diabetes Capital of the world,” but this crown is now shifted to China with a population of people with diabetes around 110 million in 2017 as opposed to 72 million in India. However, in India, Chandigarh has the highest prevalence of diabetes of 13%, as opposed to the national prevalence of 7.3%. Therefore, it can be aptly called as China the “Diabetes Capital of the world” and Chandigarh the “Diabetes Capital of India.”[2]

Economic transition, consumption of calorie-dense food, adherence to a sedentary lifestyle, and rising incidence of obesity are contributory for this enormous increase in the prevalence of disease.[3]

Prevention of diabetes is the key to halt the menace of this disease. Numerous studies have examined the impact of lifestyle modification and/or insulin sensitizers including metformin and thiazolidinediones on the prevention of type 2 diabetes mellitus (T2DM) in individuals with prediabetes. The most cited one is the Diabetes Prevention Project, which enrolled 3234 patients, and the intervention modalities included lifestyle change and metformin and troglitazone with a follow-up of 2.8 years. The study revealed that lifestyle changes resulted in risk reduction of diabetes by 58%, whereas metformin and troglitazone decreased the risk by 31% and 75%, respectively.[4] Further, the study was extended over the next 15 years, and it showed 37% reduction in the incidence of diabetes in lifestyle intervention group while 18% in the metformin group, suggesting sustained benefit over the extended period. Moreover, the people who developed diabetes had 28% higher microvascular complications than those who did not develop diabetes, indicating the beneficial effect of preventing diabetes.[5] Another study which also exhibited the importance of lifestyle changes in the prevention of T2DM is Da Qing IGT and Diabetes Prevention Study, in which patients were followed up for 6 years and showed risk reduction for diabetes by 31%–46%.[6] For the prevention of diabetes, early diagnosis of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) is warranted and this can be accomplished by screening individuals who are at high risk. Screening program encompasses all individuals above the age of 45 years, and high-risk individuals including body mass index ≥25 kg/m², those who have a family history of diabetes, women with polycystic ovarian disease and gestational diabetes, or babies weighing 4 kg at birth should also be screened, irrespective of age.[7] Other studies exploring the impact of different interventions on the prevention of diabetes are summarized in Table 1.[8–12] Therefore, lifestyle modifications may play a pivotal role in the prevention of T2DM, though difficult to sustain for a longer time. However, long-term adherence to lifestyle interventions may reap health benefits for an extended period of time. Further, addition of metformin along with lifestyle modification may not be so rewarding, although the available data are not robust.

Nevertheless, once diabetes sets in, it progressively and silently destroys every organ of the body with consequent long-term micro- and macrovascular complications, resulting in the accumulation of multiple comorbidities. Therefore, early diagnosis of diabetes, adherence to

Table 1: Studies on prevention of type 2 diabetes mellitus

| Study                                | Number of patients | Follow-up (years) | Risk reduction strategies                        | Reduction in new-onset T2DM |
|--------------------------------------|--------------------|-------------------|--------------------------------------------------|-----------------------------|
| DPP[4]                               | 3234               | 2.8               | Metformin, lifestyle change, troglitazone         | 31%, 58%, 75%               |
| Finnish Diabetes Prevention Study[4] | 522                | 3.2               | Intensive lifestyle change                        | 58%                         |
| Da Qing IGT and Diabetes Study[4]    | 577                | 6                 | Diet and/or exercise                              | 31%–46%                     |
| STOP-NIDDM[9]                        | 1400               | 3.9               | Acarbose                                          | 25%                         |
| TRIPD[10]                            | 266                | 2.5               | Troglitazone                                      | 56%                         |
| XENDOS[11]                           | 3304               | 4                 | Orlistat                                          | 37%                         |
| IDPP[12]                             | 531                | 2.5               | LSM                                               | 28.5%                       |
|                                      |                    |                   | Metformin                                         | 26.4%                       |
|                                      |                    |                   | LSM + metformin                                   | 28.2%                       |

T2DM - Type-2 diabetes mellitus, DPP - Diabetes Prevention Project, IDPP - Indian Diabetes Prevention Programme, LSM - Lifestyle modification

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lifestyle modification schedule, timely initiation of intensive treatment, periodic screening for diabetic complications, and regular monitoring of blood glucose, blood pressure, lipids, and urinary albumin can help improve the quality of life with increased longevity. However, it is only possible to effectively prevent diabetic micro- and macrovascular complications if intervened early, rather than late and aggressive treatment.

Lifestyle modification is pivotal not only for patients with diabetes but also for any individual who wants to remain healthy. Several diet programs have been recommended, but the healthy diet composition includes consumption of complex carbohydrates, an optimal amount of protein and mono- and polyunsaturated fatty acids along with three to five servings of fruits and green vegetables, which is essential for combating rising oxidative stress and restoration of “favourable metabolic profile”. Brisk walk for 30 minutes, 5 days a week not only maintains a good cardio-respiratory fitness, but also helps in restoring muscle mass, coordination and stability. Exercise-timing also influences glycaemic profile as postmeal exercise is more effective in normalizing blood glucose profile than premeal exercise. However, both exercise schedules have similar benefits on cardiovascular outcome.[13] Besides this, exercise is a great stress buster and keeps you cheerful by increasing central opioid tone. An Optimal amount of sleep is also essential for the healthy lifestyle and keeps you active throughout the day. Further, sitting for long hours should be avoided as rightly said: “sitting is killing.” Therefore, after every 1 h, 5 min physical movement should be accomplished to counteract the burden of proinflammatory cytokines. This can be further augmented by accomplishing yoga and meditation twice a week.

Early diagnosis of diabetes helps in achieving the glycemic targets faster with lesser number of pills and is inexpensive in terms of expenditure incurred on the management of long-term complications. However, many people after the diagnosis of diabetes usually insist only for lifestyle modifications and/or prefer to adapt an alternative system of medicines (e.g., herbs). Therefore, as these strategies are ill-sustained and benefits of alternative medicines for long term are uncertain, it eventually results in enhanced cumulative glycemic burden and consequent long-term complications of diabetes. A recent study also demonstrated that mitophagy, a cell-reparative process is impaired in patients with T2DM and attainment of good glycemic control (HbA1C < 7 % ) is associated with the sustenance of mitophagy.[14] Hence, early and intensive initiation of treatment not only helps control blood glucose faster and in an easier manner but can also be sustained for a long time with minimal use of medications.

Further, regular monitoring of blood glucose is pivotal to assess the glycemic control and for the prevention of diabetic complications. It also allows an individual to involve in his/her own care, thereby encouraging to achieve the desired targets and subsequent prevention of comorbidities. In addition, the control of diabetes involves not only the control of blood glucose and HbA1C but also the normalization of blood pressure and lipids, maintenance of ideal body weight, and physical fitness. All these comorbidities are to be effectively dealt to prevent diabetic complications.

Regular screening for diabetes-related complications at the time of diagnosis, and thereafter annually is crucial for effective prevention or delaying the progression of these complications. Further, regular visit of the patients to their consulting physicians at a scheduled time provides them an opportunity to interact as well as to recognize new-onset complications, which can be effectively treated even from the beginning. This also allows the reinforcement of lifestyle modification at every visit, thereby enabling them to lead a better quality of life.

Even on relentless emphasis on prevention of diabetes, some studies have explored the relevance of early and intensive intervention and late and aggressive treatment in patients with T2DM. The United Kingdom Prospective Diabetes Study[15,16] and Kumamoto study[17] demonstrated that early and intensive treatment of T2DM resulted in significant reduction in microvascular complications during 7 and 5 years follow-up, respectively, and further exhibited the “legacy effect” of good glycemic control on macrovascular complications with long-term follow-up.[18] However, other studies, which were designed to evaluate the effect of late but intensive intervention, including Action to Control Cardiovascular Risk in Diabetes,[19] Action in Diabetes and Vascular Disease (ADVANCE),[20] and Veterans Affairs Diabetes Trial,[21] demonstrated increased cardiovascular mortality possibly due to recurrent hypoglycemia, except in ADVANCE study which showed good glycemic control halted the progression of nephropathy.

Therefore, it is apt to conclude that lifestyle changes and/or metformin are better options to prevent the progression to T2DM, as preventing the disease is much easier and is associated with lesser accumulation of comorbidities, and virtually inexpensive. Nevertheless, if the disease sets in, it may be tamed by early and intensive intervention, rather
than late and aggressive treatment, which may be more detrimental than beneficial. Further, regular follow-up, periodic screening for complications, a timely action for prevention, or halting the progression of comorbidities may result in increased longevity in patients with T2DM.

Anil Bhansali, Shipra Bhansali
Department of Endocrinology, PGIMER, Chandigarh, India

Address for correspondence: Prof. Anil Bhansali, Department of Endocrinology, PGIMER, Chandigarh - 160 012, India.
E-mail: anilbhansaliendocrine@gmail.com

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