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INTRODUCTION

Diabetes has assumed pandemic proportions. In India, diabetes mellitus occurs at least a decade or two earlier than the Western world where it occurs in adults > 50 years of age. Therefore, diabetes affects the productive age group in India, and the complications too occur earlier. The prevalence of diabetes in India is reported to be 12% in the urban and 5% in the rural population, but of late, with increasing urbanisation, the urban-rural difference is narrowing. India thus, faces a major socio-economic burden due to diabetes. An equal number of pre-diabetes population exists in India, which has the potential to add-on to the existing diabetes population in the future, compounding the burden of diabetes and its socio-economic impact manifold.

With no cure in sight for diabetes, it is imperative that one makes efforts to prevent diabetes. From an epidemiological perspective, prevention of diabetes can be done at various levels-

- i. Primary prevention of Diabetes- Prevention of onset of diabetes in an individual.
- ii. Secondary prevention- Prevention of progression of diabetes and prevention of onset of complications.
- iii. Tertiary prevention- Prevention of progression of diabetes-related complications and their prompt management including rehabilitation.

Primordial prevention is promotion of a healthy life-style and is aimed at controlling the risk factors for development of diabetes, thus preventing the development of diabetes at the community level. By promoting a healthy-lifestyle and controlling the risk factors, as part of primordial prevention, we can prevent onset of a number of other lifestyle diseases too, viz. hypertension, obesity, coronary artery disease, etc.

Type 1 diabetes mellitus (T1DM) offers limited scope for prevention in view of an incomplete understanding of the disease pathogenesis and heterogeneity, and the risk factors are also largely unknown, besides validated biomarkers for precise staging of the disease are lacking. Moreover, type 1 diabetes contributes to only 5% of the total diabetes pool in our country. Primary prevention of T1DM should target the general childhood population with vaccines (viral or tolerogenic) or by altering microbiota-induced immunoregulation. Secondary

prevention will likely require combination therapies (anti-inflammatory agents, immunomodulatory agents, beta cell survival agents, and/or agents improving glucose control) used sequentially or simultaneously to preserve residual beta cell function and prevent symptomatic disease. Unlike type 1 diabetes, type 2 diabetes mellitus (T2DM) has a long asymptomatic pre-clinical period, has established risk factors where intervention is possible, and constitutes 95% of the diabetes pool in our country. Therefore, primary prevention of type 2 diabetes is plausible and there have been several studies which have tried to prevent the onset of type 2 diabetes from the prediabetes state. This article will try to restrict discussion to primary prevention of diabetes, since the secondary and tertiary prevention aspects would be discussed in detail by other authors, and moreover, including those aspects would make this write-up too exhaustive. Suffice it to say, that recent trials have confirmed that a good control of diabetes can prevent microvascular complications of diabetes. Although there is a reduction in macrovascular complications but the figures are not statistically significant. It has also been observed that some of the complications especially macrovascular complications may antedate the overt manifestation of diabetes. This is another major reason for concentrating on prevention and early screening for diabetes.

As already stated, type 2 diabetes can have a long and variable period of insulin resistance before diabetes is diagnosed, so it is an advantage in the sense that this stage can be aimed for prevention but it is also a handicap since it requires a long duration of clinical trials to see the effect of any intervention. In recent times a series of trials with lifestyle measures and/or pharmacotherapy attempted prevention of diabetes in individuals at high risk with considerable success and favourable results.

STRATEGIES FOR PREVENTION OF DIABETES

Two major strategies have been evaluated for reducing the incidence of diabetes, i.e. lifestyle interventions and drugs (pharmacotherapy). These are aimed at changing the risk factor profile of diabetes mellitus. Diabetes risk factors can be classified into modifiable risk factors and non-modifiable risk factors (Table 1). The modifiable risk factors are the subject matter of intervention.

The present epidemic of diabetes is very significantly fuelled because of growing problem of overweight and

Table 1: Risk factors for diabetes

Modifiable	Non-modifiable
Overweight and obesity	Ethnicity
Sedentary lifestyle	Family history
Previously identified impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)	Age
Metabolic syndrome	Gender
Hypertension	History of gestational diabetes mellitus
Dyslipidemia	High-birth weight baby (>4kg)
Dietary factors	
Drugs viz. corticosteroids, diuretics	
Inflammation	

*Intrauterine environment and Polycystic ovarian disease can be possibly kept as modifiable risk factors, since dietary factors and medications can help reduce the risk of diabetes.

morbid obesity, which also is a major global health problem. Excessive truncal adiposity is very well correlated with the risk for diabetes, hypertension and cardiovascular disease. The other important reason in the changing lifestyle is the lack of physical activity. This is associated with stress at work. To sum it up there is a marked increase in the intake of energy dense food with very little or no physical activity. Therefore, the question arises whether we can prevent type 2 diabetes by lifestyle interventions?

NUTRITION

In the prospective Nurses' Health Study conducted in 84941 female nurses followed for 16 years, a series of risk factors related to dietary behaviour, physical activity, weight and cigarette smoking were identified and targeted, and this was associated with a remarkable 91% reduction in the risk of developing diabetes. Even with a family history of diabetes the risk reduction was 88%. In theory, therefore, diabetes can be prevented, largely by lifestyle changes irrespective of genetic background. Some pioneering studies showed that this is feasible.

In case of over-weight individuals reduction of weight by restricting calories and increasing exercise is of vital importance. However it has been observed that it is not necessary to reduce the weight to the level of ideal body weight; but a reduction of about 5-10% in the body weight gives substantially good results.

Physical Activity

Physical activity is important both in the prevention as well as the management of diabetes in all its stages. It is recommended that around 30-40 minutes of aerobic activity like brisk walking should be encouraged for at least 5 days a week and preferably for all 7 days (equivalent to 150 minutes/week). The beneficial effects of physical activity are manifold viz. improved insulin

sensitivity, reduction in overall adiposity and central obesity, improved glucose tolerance, and increased vitality.

It is universally accepted that sticking to an exercise schedule over the years is difficult. However, a combination of dietary modification and physical activity is considered the best bet for prevention of diabetes and for health promotion.

Lifestyle Interventions

Lifestyle measures which include medical nutrition therapy and physical activity aim to address the issue of overweight and obesity, improve insulin sensitivity, prevent progression of impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) to overt diabetes and control inflammation.

The Swedish Malmo study was one of the earliest lifestyle intervention studies for the prevention of type 2 diabetes and was conducted in male subjects aged 47-49 years. Men who participated in the lifestyle intervention had a lower incidence of type 2 diabetes and a greater reversal of glucose intolerance compared to those men who received usual care. At the end of 12 years, the IGT men who underwent lifestyle intervention had similar mortality as compared to normal glucose tolerance men, but had less than half the mortality rate when compared to IGT men who received usual care.

The Chinese Da Qing study showed that diet intervention alone was associated with a 31% reduction, while the exercise alone showed a 46% reduction in the risk of developing type 2 diabetes. However, the combined diet and exercise group had a similar 42% reduction in the risk of developing type 2 diabetes during a 6-year follow-up period.

In the Finnish Diabetes Prevention Study (DPS), weight loss in overweight subjects with impaired glucose tolerance, averaging just 3-4 kg over 4 years, led to improvement in measures of lipemia and glycemia, and reduced diabetes risk. At 2-year follow-up, incidence of type 2 diabetes in the intervention group was less than half that observed in the control group. It was also reported that the impact of lifestyle changes in reducing incidence of diabetes was maintained for at least 4 years after the intensive intervention finished.

A similar result was achieved in the Diabetes Prevention Program (DPP) in the United States, in which lifestyle intervention involving exercise and dietary change over a 3-year period in subjects with impaired glucose tolerance reduced incident diabetes by 58%.

Although the results of these lifestyle intervention programmes look impressive, but in routine day-to-day practice, lifestyle management is not easy to execute, as these interventions are labour intensive, and moreover, the results may not be as replicable as to a research setting, even in well-funded healthcare systems.

Pharmacotherapy for Prevention

Considerable interest has been focused on the prevention

Table 2: Review of Pharmacological Interventions for Prevention of Diabetes

Study	Drug	Relative risk reduction (%)	Duration of study (years)
DPP	Metformin	31	3
India DPP	Metformin	26	3
DPP	Troglitazone	75	1
STOP- NIDDM	Acarbose	25	3
Xendos	Orlistat	37	4
DREAM	Rosiglitazone	60	3

of diabetes with the use of drugs which are used for the treatment of diabetes as well. Table 2 gives the important drug trials in prevention of type 2 diabetes. For instance, the Diabetes Prevention Programme Research Group study found a 31% reduction in the incidence of diabetes with metformin (at 2.8 years). Previously troglitazone was shown to be effective in controlling blood sugar levels but had to be withdrawn because of serious liver toxicity during the TRIPOD (TROglitazone In Prevention Of Diabetes) study. In people with obesity, orlistat (pancreatic lipase inhibitor) has been shown to reduce the risk of diabetes by 37% when compared with placebo.

PREVENTION IN THE INDIAN CONTEXT

The Indian Diabetes Prevention Programme (IDPP) was the first study to show that lifestyle modification was effective in preventing diabetes in native Asian Indians. IDPP was a randomised, controlled, 3-year prospective community-based study in native Asian Indian subjects with IGT. These were younger, leaner and more insulin resistant than the other populations studied (multiethnic American, Finnish and Chinese populations). The study groups were as follows: Group 1, control group with no intervention (n=133); Group 2, subjects advised with lifestyle modification (n=120); Group 3, subjects treated with 500 mg of metformin (n=128); and Group 4, subjects treated with both lifestyle modification plus metformin (n=121). The median follow up period was 30 months and the 3 year cumulative incidence of diabetes was 55%, 39.3%, 40.5% and 39.5% in groups 1 to 4, respectively. The relative risk reduction in lifestyle modification (28.5%; P=0.018), metformin (26.4%; P=0.029) and lifestyle modification + metformin (28.2%; P=0.022) compared with the control group was very similar. The study showed that progression from IGT to diabetes was high in native Asian Indians. Both lifestyle modification and metformin were equally effective and there was no added benefit from combining them.

The study thus showed that primary prevention of diabetes was possible in a comparatively lean, but highly insulin resistant Indian population by moderate changes in physical activity and diet. Screening for glucose intolerance for preventive measures at an early age is a requisite in Indians, as they develop hyperglycaemia at a younger age. It is ideal to achieve primary prevention of type 2 diabetes by means of a non-pharmacological intervention in the relatively lean Asians compared with Western population.

The Diabetes Community Lifestyle Improvement Program (D-CLIP) study published recently (August 2016) also reinforced the proven benefits of lifestyle intervention with the addition of metformin, when required. D-CLIP was a randomised controlled translational trial of 578 overweight/obese Asian Indian adults with prediabetes (impaired fasting glucose and/or impaired glucose tolerance) from Chennai, India, and were randomised to standard lifestyle advice (control group) or US DPP-based lifestyle curriculum plus stepwise addition of metformin 500 mg bid. During 3 years follow-up, 34.9% of control and 25.7% of intervention participants developed diabetes, relative risk reduction (RRR) was 32%, and the number needed to treat one case of diabetes was 9.8. Further the study reported that RRR was lowest 12% for the impaired fasting glucose (IFG) group as compared to 31% for the impaired glucose tolerance (IGT) group and 36% for the combined IFG+IGT group. Notably, most participants (72%) required metformin in addition to lifestyle.

IDF Consensus on Targeting Population in various Countries

WHO and other member countries who are seized with the problem of chronic diseases especially Diabetes have formulated a series of guidelines for implementation at the community level for the control of Diabetes. IDF has also given its guidelines. The approach with each country and subpopulation will vary from region to region. However, the basic plan of prevention will remain the same globally.

The prevention strategies can be grouped in three steps:

- Identification of People at High Risk: Large population based surveys may not be cost-effective strategy and therefore identification of people at high risk is a useful and cost-effective exercise. This is based on a screening questionnaire, which can be based on weight, waist circumference, age, gender, family history of diabetes, diet and physical activity.
- Identify These People at High Risk and Grade Them: According to the level of their risk as determined by the screening questionnaire, the individuals need to be further graded, so that groups requiring interventions can be identified, based on their relative risk category. This requires blood sugar/HbA1c testing and may be other indices of atherosclerosis and dyslipidemia.
- Interventions: The possible role of interventions

(lifestyle and/or metformin, and other drugs) has been discussed already, and the groups decided to be intervened should be initiated accordingly.

Various diabetes risk scores have been formulated and it has been found that the parameters vary from continent to continent and therefore the parameters to be used for Asian Indians are different from the Caucasian populations.

A simplified Indian Diabetes risk Score (IDRS) has been developed and is in vogue.

The information for these risk factors (IDRS) can be obtained based on four simple questions and one anthropometric measurement namely waist circumference. The four questions are:

1. What is your age?
2. Do you have a family history of diabetes? If yes, does your father or mother or both have diabetes?
3. Do you exercise regularly?
4. How physically demanding is your work [occupation]?

It gives a minimum score of 0 and a maximum of 100, with a score ≥ 60 suggesting a higher risk of developing diabetes, and in this scenario the individual should get blood sugar or HbA1c tested as a screening for Diabetes.

With advent of newer pharmacological agents viz. DPP-4 inhibitors and SGLT-2 inhibitors in the last decade, their role will also soon be investigated in the primary prevention of diabetes. In fact, the Sitagliptin and Metformin in Prediabetes (SiMePreD) study is on the anvil, wherein the effect of sitagliptin and metformin on progression from prediabetes to type 2 diabetes will be ascertained. It will be a randomised double-blind multicentric clinical study over a period of 5 years and is presently in the process of acquiring research funding.

CONCLUSION

The evidence base for prevention of diabetes mellitus is quite robust with risk factor based identification of individuals followed by confirmation of their prediabetes stage (IFG or IGT or both, or HbA1c between 6-6.5%). Lifestyle interventions- diet and activity, although difficult to adhere to in the long run, are better than use of pharmacological agents. Among the pharmacological agents, metformin is the most studied and robust,

although acarbose and orlistat also have evidence in their favour. Newer agents viz. the DPP-4 inhibitors may be suitable candidates, alone or as an adjunct, but results from newer trials only can provide the evidence in their favour.

Exercise and Nutrition counselling in office visits, at society level, at the level of school children and college students will go a long way in promoting healthy lifestyle and preventing diabetes mellitus. Providing healthy food alternatives, encouraging and rewarding physical activity in formative years are measures which need to be adopted to prevent diabetes in the community setting.

The approach should therefore focus on both the population at large by generic measures and focused measures as outlined in high risk group and in individuals in clinical setting.

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