Diabetes has been recognized from antiquity. For last 4 or 5 decades there has been worldwide increase in the prevalence of diabetes. India is no exception. It is worth noting that in India the prevalence of diabetes in the urban population has doubled in last 25 years1,2. Projection of International Diabetes Federation (IDF) is something to be noteworthy. Global projection of diabetes in 2025 by IDF suggests that India is going to have almost 60 million diabetics (i.e. more than double the population of diabetes at present). Change of food habits, more number of migrated population in the cities; sedentary life style, increase in obese population and lowering of diagnostic criteria for the diagnosis of diabetes are among the major reasons of the so called pandemicity of diabetes today.

In India, ninety eight per cent of all diabetic patients have type 2 diabetes mellitus. The micro vascular (retinopathy, nephropathy and neuropathy) and macrovascular (coronary artery disease, cerebrovascular disease and peripheral vascular disease) complications pose a serious threat to the morbidity and mortality of diabetic population. It is a serious challenge to the physician and the health care system. The very objective of treating a diabetic patient is to prevent the long term complications encountered in a diabetic subject.

The most important job of a physician is to diagnose diabetes early, so that by taking appropriate therapeutic measure and proper monitoring the complications can be prevented or delayed. The answer to the question, when to start? The answer is- start as early as possible.

Several reports including that of Diabetes control and Complication Trial (DCCT), United Kingdom Prospective Diabetes Study (UKPDS) and Steno 2 trial clearly suggest that long term complications can be prevented or delayed if intensive treatment is given to diabetic patients to keep blood sugar, blood lipids and blood pressure under control 4,5,6.

In clinical practice, however, diabetes is diagnosed late and somewhat arbitrarily on the basis of glucose level associated with appearance of characteristic long term complications, especially retinopathy and that is the basis of the diagnostic criteria of diabetes mellitus widely followed today, i.e. the blood sugar values correlating with the appearance of retinopathy and not the standard statistical formula of abnormality in the population remaining above the two standard deviation of the mean value blood sugar of the population. Before 1979 when the National Diabetes Data Group’ and later WHO EXPERT COMMITTEE 1980’ defined the upper limit of blood sugar; the diagnosis of diabetes was rather a chaos and higher blood sugar values were ill defined.

Asymptomatic patients were reluctant to diagnose their metabolic abnormality; there physicians unfortunately had much confusion as to what represents an abnormal blood glucose level. Several diagnostic criterias were in vogue as stated below.9

**Criteria for Diagnosis of abnormal glucose tolerance**

<table>
<thead>
<tr>
<th>Criteria based on plasma glucose</th>
<th>Fajans and conn* 1 hr - &gt; 185 1 ½ hr - &gt; 160 2 hr - &gt; 140 All three values abnormal for Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPHS-Wilkerson†</td>
<td>Fasting - &gt; 130=1 point 1 hr - &gt; 195=½ point 2 hr - &gt; 140=½ point 3 hr - &gt; 130=1 point points for abnormal values; 2 points for diagnosis</td>
</tr>
<tr>
<td>ADA‡ 40 g/ m²</td>
<td>Fasting - &gt; 115 1 hr - &gt; 185 1 ½ hr - &gt; 165 2 hr - &gt; 140 Elevated fasting or all three values abnormal for diagnosis</td>
</tr>
<tr>
<td>Pregnancy- O’Sullivan§</td>
<td>Fasting - &gt; 105 1 hr - &gt; 190 2 hr - &gt; 165 3 hr - &gt; 145 Two or three values abnormal for diagnosis of gestational diabetes</td>
</tr>
<tr>
<td>Children – Seltzer 1.75 g/kg</td>
<td>Capillary whole blood Fasting - &gt; 115 1 hr - &gt; 175 2 hr - &gt; 140 3 hr - &gt; 125 Elevated fasting or two of three post-test values abnormal for diagnosis</td>
</tr>
</tbody>
</table>
Many diabetic patients have poor diabetic control and are prone to micro and macrovascular complications. While the cause of inadequate management are complex, the problem is due in part to recognition relatively late in the natural history of glucose intolerance. As beta cell function and mass are lost gradually, it becomes progressively more difficult to lower glucose level to normal.

It goes without saying that ideal time for intervention is the pre-diabetic stage and if possible even before that when a person with normal blood sugar is overweight, having a sedentary lifestyle, hypertensive or having a diabetic in the family. In fact, detection earlier in the natural history of diabetes would be more beneficial. At this stage of prediabetes one can enable lifestyle change and/or pharmacologic agents to keep glucose level near normal, prevent or delay the development of diabetes, and improve the cardiovascular risk factors.

Identify the Undiagnosed Cases

Identifying the undiagnosed diabetic and pre-diabetic population is the most difficult but the most important job. Though very little we can do to the non-modifiable risk factors; like genetic factors, age and gender, past history of gestational diabetes mellitus (GDM); we can definitely plan to approach the modifiable risk factors, like obesity, physical inactivity, nutritional factors. To identify undiagnosed cases, screening the following group of population who has high risk of developing diabetes are very important

Overweight or obese
Sedentary lifestyle
Family history of diabetes
IGT, IFG, Metabolic Syndrome

### WHO Diabetes criteria - interpretation of Oral Glucose Tolerance Test

<table>
<thead>
<tr>
<th>Glucose levels</th>
<th>WHO Diabetes criteria - interpretation of Oral Glucose Tolerance Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous plasma</td>
<td>Fasting 2 hrs</td>
</tr>
<tr>
<td>(mmol/L)</td>
<td>&lt; 5.5</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>&lt; 100</td>
</tr>
</tbody>
</table>

National Diabetes Data Group (NIH)
- 0.5, 1.0, or 1.5 hr -> 200 and 2 hr -> 140
- Both values abnormal for diagnosis 75 g to all subjects of impaired glucose tolerance
- Diabetes = Fasting -> 140 or 2 hr and 0.5, 1.0 or 1.5 hr -> 200
- Children -> 140 for diagnosis of impaired glucose tolerance

Today there is wide acceptance to the fact that there is a continuous spectrum of glucose levels between those considered normal and those to be considered as diabetic. A fasting plasma glucose < 100 mg/dl and 75 gm post glucose 2 hrs value < 140 mg/dl is considered normal. and a fasting ≥ 126 mg/dl and post glucose 2 hrs value ≥ 200 mg/dl are diagnostic of diabetes. There has been a ‘gap’ between the normal and a diabetic blood sugar value, so that normal persons are not given the label of diabetes, a degenerative metabolic disease with so much of restrictions and monitoring.

**Prediabetes**

It has been observed by many that at the time of diagnosis a good number of new diabetic patients already have long term complications. These observations suggest that they were having diabetes from a much early period and remained asymptomatic and so undiagnosed. or long term complications may start even earlier in a subject who do not satisfy the criteria of diabetes but are having blood sugar higher than the normal range.

This range of blood sugar in between i.e. fasting plasma glucose between 100 and 125 mg/dl (called impaired fasting glucose or IFG) and 2 hours post 75 gm glucose plasma sugar value between 140 and 199 mg/dl (called impaired glucose tolerance or IGT) are taken as PreDiabetes.

The patient should have been fasting for the previous 8—14 hrs (water is allowed)

No smoking.

The progression of diabetes from IGT is 6% to 10% per year and the risk is more when a subject has both IFG and IGT. The risk of coronary artery disease (CAD) maintains a linear correlation with glycemia well below the present diagnostic criteria of diabetes mellitus. Approximately half of patients with IGT meet this NCEP (National Cholesterol Education Programme) criteria for the diagnosis of metabolic syndrome. This syndrome of multiple cardiovascular risk factors characterizes a group of individuals at increased risk of diabetes, as well as Coronary Artery Disease (CAD). Thus, IFG, IGT and metabolic syndrome may each describe a pre-diabetic state that has coincidental CAD risk.

**Start Early**

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Sedentary lifestyle
Family history of diabetes
IGT, IFG, Metabolic Syndrome
Pre-diabetes or Diabetes: When to Start?

Hypertension
Dyslipidemia
History of gestational diabetes
Polycystic ovary syndrome
Receiving antipsychotic or antidepressants

Several studies suggest that patients with IGT are at risk and if untreated they progress to the state of diabetes, as well as micro and macrovascular risk. In the DPP (Diabetes Prevention Programme) diabetic retinopathy was observed in 7.9% of subjects with IGT compared to 12.6% in those who later developed diabetes. In the untreated IGT group hypertension and dyslipidemia progressed from 29% to 38% and 6% to 16% respectively. In a recent analysis of the San Antonio Heart Study - those who later converted to diabetes from pre-diabetes had significantly higher BMI, waist circumference, triglyceride level and lower HDL concentration. The pre-diabetic state is considered to be atherogenic.

Management of Prediabetes

Management approach involves a set of measures designed to address its abnormalities and cardiometabolic risk factors. As the pre-diabetes progresses drug therapies directed towards hyperglycemia and the individual coronary artery disease risk factors may be required. Strict control of all known risk factors of CAD and microvascular complication in a type 2 diabetes by aggressive management of hypertension, dyslipidemia and glycaemia has proved beneficial. Glucose directed therapeutic approach alone will not be sufficient for pre diabetes. The failure of late treatment strengthens the argument in favour of early treatment, that is-at the stage of pre diabetes.

Life style modification is the cornerstone of management, it should be reinforced in every visit of the patient to the clinic. Lifestyle is the fundamental management approach that can effectively prevent or delay progression of pre-diabetes to diabetes, as well as reduce both microvascular and macrovascular disease risks. Lifestyle intervention improves components of metabolic syndrome (e.g., obesity, hypertension, dyslipidemia and hyperglycemia).

Emphasis should be given to weight loss in over weight pre-diabetic subjects. Diabetes Prevention Programme findings indicate that 5 to 10% weight loss will be beneficial. Importance should be given to long term maintenance after reducing the body weight. Modest degree of weight loss, results in decreased fat mass, blood pressure, glucose, LDL-cholesterol and triglycerides. These benefits can also translate into long term outcome, especially when they are maintained.

Nutritional factors: Much uncertainty still surrounds the dietary factors involved in developing diabetes. Nutritional factor leading to overweight, body fat e.g., higher total calorie, high glycemic load, high saturated fat always should be avoided in daily meal plan for pre diabetes.

Life style management may be difficult to maintain, but the following have been shown to increase the likelihood of success:

- Patient self-monitoring
- Realistic and stepwise goal setting
- Stimulus control
- Cognitive strategies
- Social support
- Appropriate re-inforcement

Physicians should focus on reinforcing maintenance of weight loss as the long term goal.

Pharmacology in pre-diabetes

Currently there is wide variation in opinion regarding the pharmacological therapy in this period of pre diabetes. Even after the diagnosis of diabetes mellitus a trial of diet & exercise for six weeks to 3 months is given by most of the physicians. Unlike diabetes where metformin is recommended, in pre diabetes no pharmacologic therapy is approved by authorities like US Food and Drug Administration. Thus, any decision to advise pharmacologic therapy is off-label and requires careful judgment regarding the risks and benefits of each specific agent in each individual patient. Several trials though, have shown beneficial effect, may be to some extent to prevent subjects of pre diabetes to go to the diabetic state.

Metformin, Alpha glycosidase inhibitors and glitazones – all have shown promising results. American Diabetic Association, Australia Diabetic Association and Indian Health Service Guidelines for case of adults with pre diabetes and/or metabolic syndrome – recommend metformin in high risk patients where there is clear evidence of glycemic deterioration, or progression of underlying disease, as evidenced by increase in FPG, HbA1c and 2 hr. PPG. The use of metformin is supported by its relative safety, cost effectiveness and long term data in several studies. The ideal pharmacological therapy must demonstrate long term safety, health benefit (reduced incidence of diabetes, microvascular and macrovascular complications and mortality), cost effectiveness and the ability to halt the biological progression from pre diabetes to diabetes. These factors will remain the subject of future research in the prevention of diabetes.

Conclusion

Prevalence of diabetes is increasing all over the world. Unfortunately approach to this grave situation both by the patients, as well as their physicians, are far from the ideal.

Diagnostic criteria of Diabetes (WHO 1997) is more or less accepted all over the globe and at present the diagnosis of diabetes has been made simplified. In spite of that there has been a great inertia on the part of patients and their physicians to treat it. Patients and physicians became aggressive in management only where there is some micro or macrovascular complications develop. If euglycemia, normal blood pressure and normal blood
lipids are maintained from the beginning of diagnosis, then only the micro and macrovascular complication could be prevented. Now that we get a large population of pre-diabetes before diabetes. The target of preventing longterm complication should be prediabetic population. All of them should be tried with lifestyle modification, weight loss programme, so that they can be prevented to have diabetes, microvascular complication and coronary artery disease. Antihyperglycemia, Anti lipid and Anti hypertensive pharmacologic agents should be given to those high risk pre-diabetics with metabolic syndrome.

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