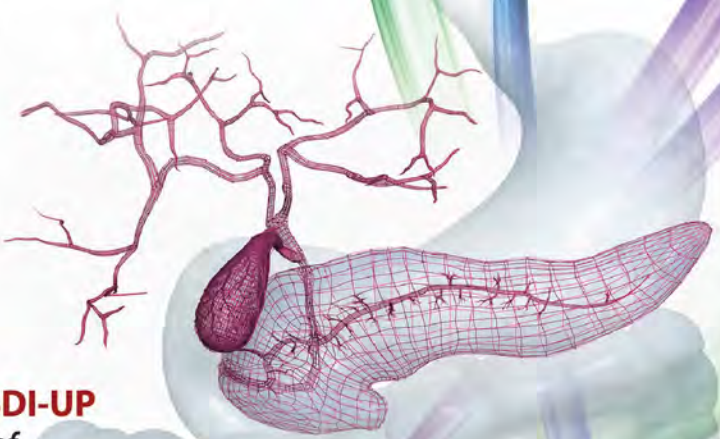
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Fundamentals of
Diabetes

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UP CHAPTER

Forewords
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2

CHAPTER

Epidemiology of Diabetes

SC Mohapatra

INTRODUCTION

Diabetes is much beyond the concept of the general population than the "*Sugar Disease*". The Chamber's Dictionary states, "Diabetes is any of several diseases marked by excess discharge of urine". Thus the prevalence of diabetes depends on how it is defined in the study. It is per se a group of diseases where there is "polyuria, polydipsia and polyphagia".

Diabetes is a known disease since 200 years, when Langerhans described the pancreatic islets in 1869 and 20 years after Minkowski experimentally produced diabetes in animal by removing the pancreas. Interestingly, the treatment of insulin for diabetes was discovered by an orthopedic team of Banting and Best in 1921, and by 2119 there will be an estimated diabetic about 387 million. As of 2010, an estimated 285 million people had diabetes, with 90% having type 2 diabetes.[1] International Diabetes Federation (IDF), estimated 381 million people having diabetes by 2013. The incidence is increasing rapidly, and by 2030 the cases will be doubled.[2]

Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries but developing countries like India and China are leading in numbers. The Western European and American incidence study by Guy's Bedford survey was the first of its kind undertaken by glucose tolerance in the community in 1962, which showed the incidence to be 13/1,000 population with 130/1,000 normal population showing blood sugar 120 mg/100 mL of blood after ingestion of 50 g glucose. Recently, the greatest increase in prevalence is, however, expected to occur in Asia and Africa, by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e. dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented. Almost one Chinese adult in ten has diabetes. A 2010 study estimated that more than 92 million Chinese adults have the disease, with another 150 million showing early symptoms. The incidence of the disease is increasing rapidly; a 2009 study found a 30% increase in 7 years.[3]

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Box 1: Global burden: Fact sheet

- In 2012, 371 million people had diabetes; the numbers is likely to increase to 552 million by 2030.
- There is a rising incidence of type 2 diabetes globally.
- Approximately 80% of diabetic subjects live in low- and middle-income countries.
- The greatest number of people with diabetes are between 40 years and 59 years of age.
- Almost 50% (183 million) diabetics are undiagnosed.

Although, both type 1 and 2 diabetes contribute to this burden, and prevalence of type 1 diabetes has also increased over the years, type 2 diabetes is the major contributor to the epidemic, contributing more than 90% of all cases of diabetes. About 78,000 children develop type 1 diabetes every year.

In Australia, the age-standardized prevalence of self-reported diabetes in indigenous Australians is almost four times that of non-indigenous Australians.[4] China followed by India has more diabetics than any other country in the world. Every 6 s a person dies. The disease affects more than 62 million Indians, which is more than 7.1% of India's adult population. An estimate shows that nearly 1 million Indians die due to diabetes every year. The average age on onset is 42.5 years. The high incidence is attributed to a combination of genetic susceptibility plus adoption of a high-calorie, low-activity lifestyle by India's growing middle class.[5] A study by the American Diabetes Association reports that India will see the greatest increase in people diagnosed with diabetes by 2030.[6] About 3 million people in the United Kingdom have diabetes mellitus, and they could become high as 6.2 million by 2035 (Box 1).

THE GLOBAL BURDEN

Majority of 382 million people with diabetes, are aged between 40 years and 59 years, and 80% of them live in low- and middle-income countries.[6] The diabetes are on the increase, and more so, type 2 diabetes. Contrast to the other estimates, the IDF states, the number of people with diabetes will increase by 55% by 2035. An additional 21 million cases of high blood glucose in pregnancy are estimated to contribute to the global burden of diabetes. In human as well as financial terms, the burden of diabetes is enormous, provoking 5.1 million deaths and taking up some 548 billion US dollars in health expenditure (11% of the total spent worldwide) in 2013 (Fig. 1). More than 21 million live births were affected by diabetes during pregnancy in 2013. Diabetes UK have also predicted that the National Health Service (NHS) could be spending as much as 16.9 billion pounds on diabetes mellitus by 2035, a figure that means the NHS could be spending as much as 17% of its budget on diabetes treatment by 2035.[7]

The Figure 2 shows the quantum of the increase of the burden from today till 2015 world over, where the African burden will be increasing more than 100%. Diabetes caused 5.1 million deaths in 2013, and it is recorded that every 6 s one person dies of diabetes. Every country is affected by diabetes mellitus today, while exact figure of other kinds of diabetes is not available today. The disease in children as well as the young adults is increasing very fast in most developing countries, probably because of change in lifestyle. This will be leading to the burden on health care needs, cost at the same time flare up in the complications of the disease. It is estimated that Southeast Asia region has 20% of the global diabetic population, and they will be tripled by 2025.[8] During last 20 years, there has been substantial increase in diabetes

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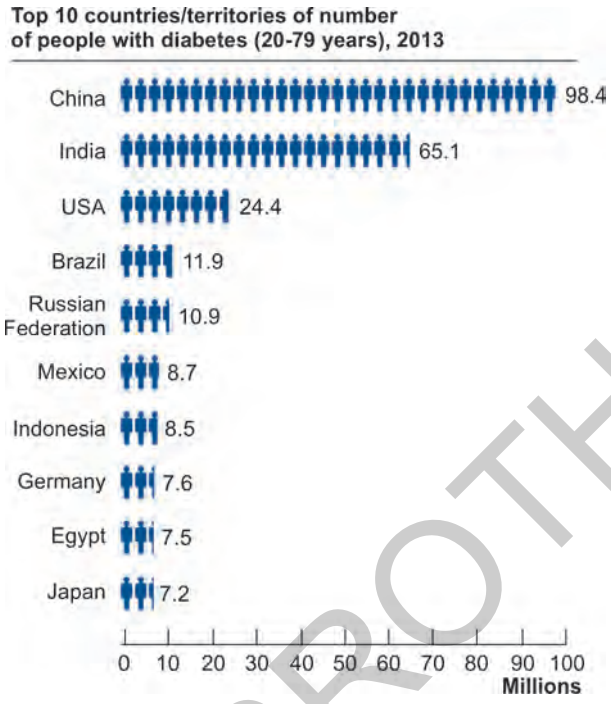


Fig. 1: Global burden of diabetes

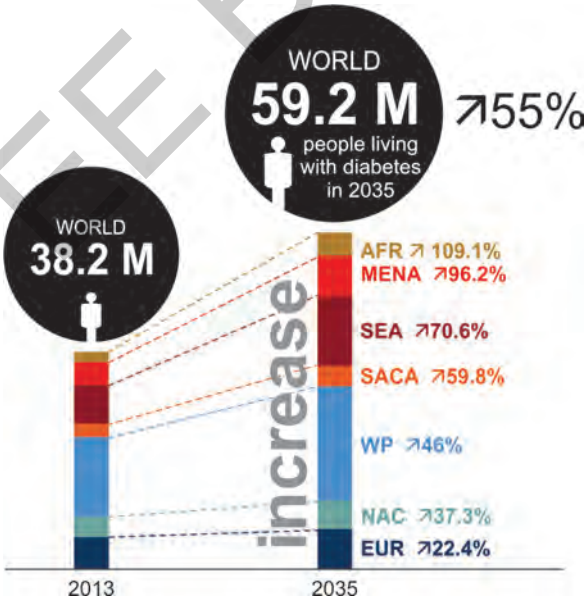


Fig. 2: Expected hike in diabetes

Abbreviations: AFR, Africa; MENA, Middle East and North America; WP, Western Pacific; SACA, South and Central America; SEA, South East Asia; EUR, Europe; NAC, North America and Caribbean

Source: International Diabetes Federation. IDF Diabetes Atlas, 6th edition. Brussels: IDF; 2014.

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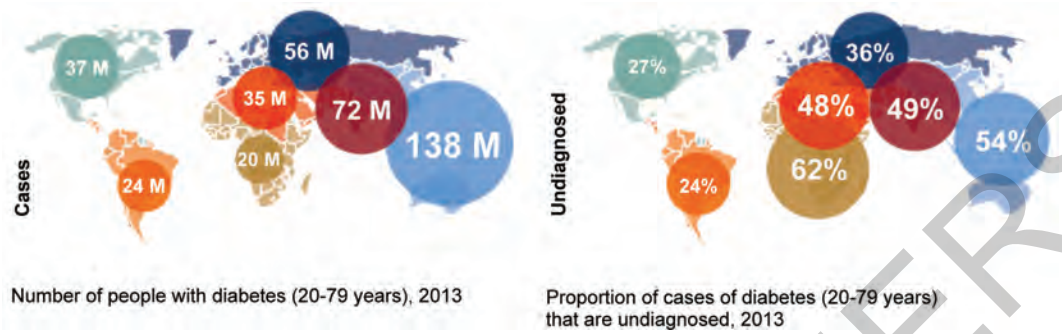


Fig. 3: Cases of diabetes world over
Source: International Diabetes Federation. IDF Diabetes Atlas, 6th edition. Brussels: IDF; 2014.

rates in the North America. In 2010, nearly 26 million people had diabetes; 7 million people remain undiagnosed and 57 million people are estimated to have pre-diabetes in the United States.[9]

The American Diabetes Association cites the 2003 assessment of the National Center for Chronic Disease Prevention and Health Promotion (Centers for Disease Control and Prevention) that one in three Americans born after 2000 will develop diabetes in their lifetimes.[10] Obesity, industrialization, acculturative nutrition and urbanizations have tremendous impact on occurrence of diabetes. The IDF states that indigenous people are especially vulnerable to diabetes. The Figure 3 as presented by IDF is being shown hereunder to highlight the problem as to how serious the problem is the diabetes is a disease of ice-berg where 50% cases remain undiagnosed, since more often than not, diabetes mellitus is diagnosed accidentally than intentionally, particularly in the developing countries where there are no scheduled screening.

EPIDEMIOLOGICAL CONCEPT IN DIABETES

At this juncture, the epidemiological interactions need to be re-defined. In diseases such as diabetes the traditional epidemiological triad does not effectively explain the causation. The host is the poor victim in any way, hence may not be included in the interaction. On the other hand, three other factors affect his health: the agent (particularly in communicable diseases), environment (including lifestyle) and genetic factors (particularly in case of noncommunicable diseases). The gene needs special mention since it could be of the human host or the agent or the vector; in other word, a factor that affects extensively and universally. The Figure 4 depicts the epidemiological quadrate for diabetes mellitus or most noncommunicable diseases, for that matter.

Thus what is essential for health care delivery system is to timely and universally identify the genetic predilection for noncommunicable diseases as primordial prevention measure in order to control disease occurrences. This has been amply proved by Cyprus as to how one nation's culture influences its genes and control disease.

The lives of Cypriots with β-thalassemia have changed over the years. Improved population genetic health care during the past decades has dramatically increased life expectancy for people with two mutations associated with β-thalassemia from 3 or 4 years to almost 30 years

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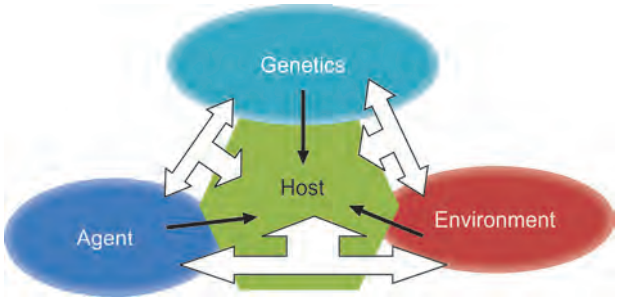


Fig. 4: Concept: epidemiological quadrate

and the prevalence has also reduced.[11] In considering the noncommunicable diseases with the glass of genetics, therefore, the modern epidemiological concept ought to have the next molding of epidemiological quadrate as explained above.

Genetics, the Epidemiological Factor

Non-insulin-dependent diabetes mellitus (NIDDM) shows strong familial aggregation. Twin and family studies have provided firm evidence that the role of the genetic component is relatively strong.[12] NIDDM appears to be the consequence of an interaction between this genetic susceptibility and exposure to environmental factors. In certain populations in which there is evidence of a major genetic component, a "thrifty genotype" has been proposed.[13] By conferring metabolic efficiency, this offers advantages in times of prolonged food deprivation but becomes disadvantageous when food is plentiful. Several genes have been suggested as markers for NIDDM but to date, apart from evidence for abnormalities in the adenosine deaminase[14] and glucokinase genes[15] in some families affected by maturity-onset diabetes of the young, no other consistent abnormalities have yet been found. However, it has become clear today that the gene is the 4th interacting component of diabetes as the epidemiological quadrate for sure. Several environmental factors have been proposed such as physical activity, poverty, nutritional factors, diet, alcoholism, stress, hormonal therapy, body weight and fat distribution, etc. The prevalence increases with age, and particularly in populations undergoing epidemiological transition—a high IGT prevalence may prelude to "epidemic" levels of NIDDM in these communities.[16] In insulin-dependent diabetes mellitus (IDDM) (type 1 diabetes) the concordance was 50%, as against 90% in NIDDM. Thus IDDM is not totally a genetic entity.[17] The IDDM genetic markers are HLA-B8, B15, HLA-DR3 and DR4 and NIDDM is not HLA associated disease.

Other epidemiological determinants include inflammatory or neoplastic pancreatic disorders, cystic fibrosis, synthesis of abnormal insulin, etc. are also partial genetic entities. However viral infections due to rubella, mumps and coxsackie are blamed to be diabetogenic.

Similarly chemical agents such as alloxan and streptozotocin and rodenticides, etc. can also damage the pancreas and produce diabetes. Age-wise, while NIDDM affects the middle aged people nutritional diabetes can be seen in younger age. Sex-wise male and female show equal diabetic load in the developing countries while in India there is male preponderances, which may be due to higher hospital attendance of the males. Obesity, particularly central deposition is accepted as a risk factor for NIDDM, as seen in India and Sri Lanka.

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Physical inactivity or sedentary lifestyle is a known risk factor for diabetes. Lack of exercise alters the relationship between insulin and its receptors, and eventually induces NIDDM. Sedentariness also acts indirectly by promoting obesity. On the other hand, low birth weight, premature baby, protein-energy malnutrition, starvation, etc. have a damaging effect on beta cells of pancreas, which impairs carbohydrate metabolism, which may progress to diabetes.

Deficiency of trace elements such as calcium, copper and zinc are suspected to induce diabetes. In some cases, controlled experimental studies have shown dietary fiber have effect in reducing hyperglycemia.[18] High and low level of diabetes has been associated with different social class and groups like many more noncommunicable diseases.

Diagnosis of Diabetes Mellitus

As per WHO,[17] the diagnostic criteria is oral glucose tolerance test (GTT) as given in the Table 1. There has been distinct difference between the type 1 and type 2 diabetes mellitus which has been given in a simplified way in the Table 2.

People of diabetes mellitus not judged clinically not to be in urgent need of insulin to preserve life are classified as non-insulin-dependent. This is classification by exclusion. NIDDM covers a wide spectrum of degrees of glucose intolerance, ranging from the totally asymptomatic to the severely symptomatic. Metabolic status may deteriorate with time or improve with treatment.

Table 1: Diagnosis of diabetes mellitus by oral glucose tolerance test

Diabetes	FPG 2hpp	≥7.0 mmol/L (126 mg/dL) or ≥11.1 mmol/L (200 mg/dL)
Impaired glucose tolerance	FPG	<7.0 mmol/L (120 mg/dL) and ≥ 7.8 and 11.1 mmol/dL
Impaired fasting glucose	2hPP FPG	140 mg/dL and 200 mg/dL 6.1 to 6.9 mmol/L 2hpp <7.8 (110 to 125 mg/dL, (140 mg/dL)

Table 2: Differences between type 1 and 2 diabetes mellitus

Features	*Type 1 diabetes mellitus*	*Type 2 diabetes mellitus*
Pathogenesis	Pancreatic damage	Insulin resistance
Age of onset	Usually <20 years	Usually ≥30 years
Presentation	Sudden	Gradual
Ketoacidosis	Common	Not common
Family trend	<10%	Common
Twin concordance	40%	100%
Acanthosis nigricans	Not seen	Common
Obesity	Not common	Common
HLA association	Common	No association
Insulin requirement	Is a Must	May be needed
Islet cell antibodies	As high as ≥85%	<5%

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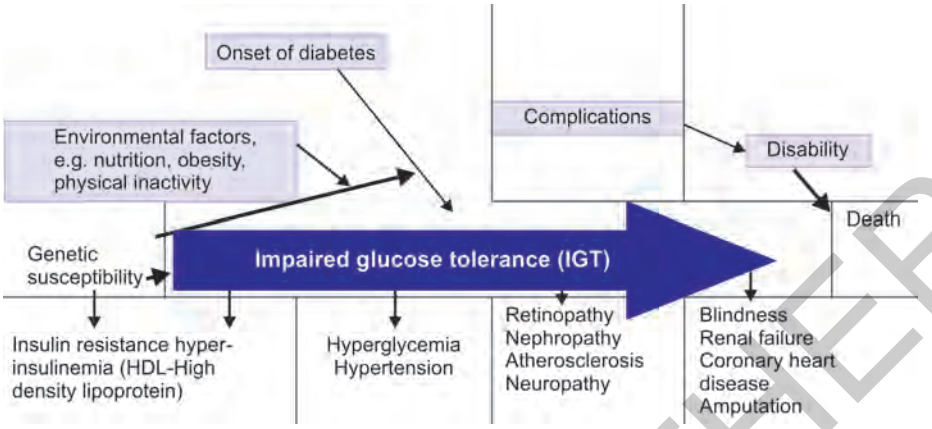


Fig. 5: The natural history of NIDDM

Source: Modified from WHO study group. WHO Technical Report Series; 844. Geneva: WHO; 1994.

The subdivision of NIDDM into obese and non-obese forms is recognized and is included in the 1985 WHO Study Group's classification. As regards Malnutrition-related diabetes mellitus, there is no association between fibrocalculous pancreatic diabetes and gallbladder disease or, in most cases, excessive alcohol intake, and no indication that the characteristic pancreatic fibrosis is postinflammatory in nature.[19] The underlying causative mechanism(s) may relate to the effect of dietary toxins against a background of long-standing malnutrition, as suggested by the association between the global distribution of fibrocalculous pancreatic diabetes and the consumption of dietary toxins in foods such as cassava root (manioc, tapioca). Further investigation is needed of the possible role of cyanogenic glycosides (e.g. linamarin) in initiating cellular injury and causing this form of diabetes when detoxifying mechanisms are inadequate because of insufficient intake of dietary protein rich in sulfur-containing amino acids. Other food toxins may play a similar role. NIDDM and IGT detected only during pregnancy, gestational NIDDM (GDM) and gestational IGT (GIGT) tend "to recur with subsequent pregnancies; GDM carries a very high risk of the ultimate development of permanent NIDDM.

There are at least three major factors of importance: (1) individual or ethnic genetic factors leading to susceptibility; (2) defects in pancreatic beta cell function; and (3) decreased action of insulin in insulin-sensitive tissues (insulin resistance), including skeletal muscle, liver and adipose tissue). The natural history of NIDDM is depicted in the Figure 5. The genetic factors are therefore important epidemiological factors beyond the typical triad, as explained earlier.

Screening for Non-insulin-dependent Diabetes Mellitus

The question of mass community screening for NIDDM remains controversial issue, since covering the whole population is operationally and administratively difficult. Technically, detection of diabetes in asymptomatic or minimally symptomatic individuals will result in effective treatment that may retard its progression and reduce the risk or the severity of complications, thus diminishing premature morbidity and mortality. The sensitivity, specificity and cost-wise diagnostic/screening tools have been depicted in the Table 3, as per WHO.[14]

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Table 3: Cost and sensitivity of screening method in diabetes

Diabetes type	*Method*	*Specificity*	*Sensitivity*	*Cost*
NIDDM*	Glycated HbA_{10} or proteins	+ + +	+/-	+ + +
	Urine glucose	+/-	+/-	+
	Casual blood glucose	+ +	+	+
	Fasting blood glucose	+ + +	+	+
	Oral glucose tolerance test	+ + +	+ +	+ +
IDDM	HLA type	+/-		+ + +
	ICA	+	+	+ + +
	Anti-GAD	+	+	+ + +
	Early insulin secretion	+/-	+	+ +

Keys: -, none; +/-, none or minimal; +, low; + +, intermediate; + + +, high.
* At present screening can be recommended only for high-risk individuals or for epidemiological studies.
Abbreviations: HLA, human leukocyte antigen; ICA, islet cell cytoplasmic antibodies; anti-GAD, antibodies to glutamate decarboxylase.

There can be population screening, which is meant for health care planning, epidemiological research or high prevalence populations. But this is not cost-effective neither cost beneficial. Thus it is recommended to undertake selective screening, taking ethnicity, positive family history, obesity and other factors such as age, previous abnormal GTT, hypertension, macrovascular disease or dyslipoproteinemia, etc. Opportunistic screening is probably one of the most pragmatic way of screening diabetes.[21] Opportunistic screening is highly cost-effective as well as convincing by counseling for the patient. For sure or not, this is the most frequently occurring diagnostic path of diabetes.

PREVENTION AND CONTROL

It cannot be too emphatically said that diabetes can be controlled, but it can definitely be reduced below the public health problem level. Taking a cue from the Western European and American incidence study by Guy's Bedford survey was the cutoff level of public health problem should be set at the incidence to be 13/1,000 population. However there is no set universally accepted cutoff level for diabetes to set as public health problem. It is increasingly accepted that diabetes is a major public health problems. Health care organizations have recognized the enormous personal and public costs of uncontrolled diabetes in terms of complications, patient quality of life and health care system resources. Multilevel systems approach addresses supportive and inhibitory social-environmental factors at multiple levels such as personal, family, health care team, work, neighborhood, community are key areas to be dealt with. The key disciplines contributing to a population-based approach to diabetes include epidemiology, behavioral science, health care services, public health, health economics and quality of life professions. Diabetes is a major public health and economic problem, affecting over 17 million Americans and costing nearly $132 billion a year.[20] The situation over the globe is almost similar with the influential deviation due to lifestyle, nutrition and the health care status.

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Primordial Prevention

The carefulness of the health system in a country is inversely proportional to the morbidity status. So is for diabetes. The health programs for prevention of maternal and fetal malnutrition, program for healthy newborn, protection of malnutrition in under-fives and protection of people from starvation are major primordial steps to be included in country's health program. Monthly or annual universal health checkup/screening for abnormalities should be the integral part of health program of all countries. This will prevent risk factors before they appear. No prevention program should be commenced without a properly constituted evaluation component of the health system. Making baseline measurements to establish the prevalence, risk factors including IGT and general and central obesity and to determine levels of physical activity and fitness and of other factors such as insulin resistance, blood lipids and blood pressure, fasting plasma insulin concentration and/or insulin sensitivity should also be assessed periodically, as a part of inbuilt health program of the country. Such step of primordial approach would help preventing many noncommunicable diseases; the component of regular, continuous and timely information collection may be increased depending on the local priority of the country. It is therefore considered as the population strategy of diabetes prevention.

Primary Prevention

This is the important prevention component for both communicable and noncommunicable diseases. As regards diabetes, strict implementation of steps of primordial prevention should be the first step in primary prevention. The other steps of preventive measure includes maintenance of body weight, adoption of healthy diet, including fiber food in daily meals, physical exercise, adopting healthy lifestyle, avoidance of alcohol, restriction on fasting and feasting, etc. The stress should be avoided with escalating spiritual wellbeing by simple Indian habits such as listening religious music, yoga and gardening particularly in the morning. Strict and regular screening of personal health is an integral protection measure of diabetes and many more noncommunicable diseases such as heart disease and cancer. Specific protection measure for type 1 diabetes is genetic counseling, which in south Asian countries, understood as nonpractical. But avoidance of sedentary lifestyle, overnutrition, alcoholism and obesity will help protecting from NIDDM. Persons in risk of diabetes, whether family history is positive, should avoid diabetogenic drugs such as oral contraceptive and chemical agents such as alloxan, streptozotocin and rodenticides, etc. Deficiency of trace elements, such as calcium, copper and zinc, need to be replenished in the subject at risk. These steps are included in the high-risk strategies for diabetes.

Secondary Prevention

It is the key measure of protective strategy in diabetes mellitus which gives emphasis on early diagnosis and adequate effective treatment. The measures include maintenance of blood glucose level close to the normal limits as far as practicable, regulate body weight to normal level, avoidance of feast and fast and adding fiber diets to meal. Regulating blood glucose level with oral hypoglycemic agents or insulin is the only curative-prevention measure. In the meantime, the patient must regularly check the blood and urine sugar, urine for protein and ketone bodies, vision, blood pressure and the kidney function. Glycosylated hemoglobin

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estimation should be undertaken every 6 months to get the long-term index of glucose control. Personal care of self and responsibility has to be the inbuilt lifestyle of the patient toward avoidance of alcohol and injury, adherence to diet and drug regimen as per medical advice, self-glucose monitoring, understanding hypoglycemia effect and reporting to the consultant timely are the key elements of protective strategy. As per WHO (2011), the Table 4 shows the efficacy of individual protective strategy.[21] Further, the woman found to have glucose intolerance during pregnancy, the high risk of the later development of diabetes[22] offers the important possibility of preventive intervention.

Table 4: The efficacy of individual protective strategy (adapted from WHO)[21]

Individual intervention with evidence of efficacy	*Benefits*
• Lifestyle intervention for preventing type 2 diabetes in high-risk people	• Reduction of 35–58% in incidence
• Metformin for preventing type 2 diabetes in high-risk people	• Reduction of 25–31% in incidence
• Glycemic control in people with HbAIc greater than 9%	• Reduction of 39% in microvascular disease per 1% drop in HbAIc
• Blood pressure control in people having blood pressure higher than 130/80 mm Hg	• Reduction of 359% in macro- and microvascular disease per 10 mm Hg drop in blood pressure
• Annual eye examination	• Reduction of 60–70% in serious vision loss
• Foot care of people with high risk of ulcer	• Reduction of 50–60% in serious foot disease
• Angiotensin converting enzyme inhibitor use in all people with diabetes	• Reduction of 42% in nephropathy and 22% drop in cardiovascular disease

It has been claimed that the vigorous treatment of GDM (gestational diabetes mellitus) with insulin during pregnancy will reduce the risk for the fetus and of overt diabetes later in life in the mother. This requires confirmation by controlled clinical trials. After pregnancy, dietary intervention to prevent obesity and physical exercise (as for prevention of NIDDM) are rational measures, but should also be the subject of planned clinical trials.

All patients of diabetes, irrespective of type 1 or type 2, should carry a personal information card showing the details for treatment, the names of person and physician for contact during any crisis. Education measures for the patient and the family members about care in diabetes are an optimizing measure of prevention and care.

Tertiary Prevention

Tertiary prevention of diabetes aims at the limiting of disability as well as increasing rehabilitation. The aim of this step is to provide capability strategy for the patients to withstand the complications which make the patient disable; such as gangrene of the lower limb, blindness, coronary thrombosis needing instant care, kidney failure or thriving over an insulin coma. The health system needs to develop specialized diabetic clinic and disability skirmishing units. The tertiary health units for diabetes must get involved in regular clinical and epidemiological research as well as public aware measures in form of mass media, print information and senior citizen aware clinics. Establishment of local and national registries have been advocated in this regards.[13] Periodic evaluation and country-wise information dissemination should also be an important national strategy.

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