Review Article

Diabetes Mellitus in India: The Modern Scourge

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Abstract

India has a high prevalence of diabetes mellitus and the numbers are increasing at an alarming rate. In India alone, diabetes is expected to increase from 40.6 million in 2006 to 79.4 million by 2030. Studies have shown that the prevalence of diabetes in urban Indian adults is about 12.1%, the onset of which is about a decade earlier than their western counterparts and the prevalence of Type 2 diabetes is 4-6 times higher in urban than in rural areas. The risk factors peculiar for developing diabetes among Indians include high familial aggregation, central obesity, insulin resistance and life style changes due to urbanization. Screening for gestational diabetes and impaired glucose tolerance among pregnant women provides a scope for primary prevention of the disease in mothers as well as in their children. The problems of obesity and impaired glucose tolerance (IGT) (important predisposing factors) are not confined to adults alone but children are also increasingly getting affected. Most long standing macro and micro vascular complications are also more common among Indian diabetics as compared to other races and ethnic groups. A strong familial clustering of diabetic nephropathy among Indian Type 2 diabetics has also been noted. Clustering of cardiovascular risk factor like Syndrome X is common among urban Indians. The rising incidence of diabetes and its complications are going to pose a grave health care burden on our country. Timely effective interventions/measures and screening tests for complications at the time of diagnosis becomes imperative not only for early detection, but also to prevent progression to end stage disease. Screening for gestational diabetes among pregnant women would also go a long way in primary prevention of the disease. Life style changes/interventions and drugs like rosiglitazone are the current strategies that can prevent and/or delay the onset of diabetes. Simple interventional strategies like "Eat less, Eat on time and Walk more" can go a long way in preventing these chronic disorders among present as well as in the future generations.

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Key Words : Type 2 diabetes; Central obesity; Insulin resistance; Gestational diabetes; Waist hip ratio; Familial aggregation

Introduction

Diabetes represents a spectrum of metabolic disorders, which has become a major health challenge worldwide [1]. The unprecedented economic development and rapid urbanization in Asian countries, particularly in India has led to a shift in health problems from communicable to non-communicable diseases. Of all the non-communicable diseases, diabetes and cardiovascular diseases lead the list.

Diabetes is pandemic in both developed and developing countries. In 2000, there were an estimated 175 million people with diabetes worldwide and by 2030, the projected estimate of diabetes is 354 million [2]. The greatest relative rise is predicted in the developing countries of the Middle Eastern Crescent, Subsaharan Africa and the Indian subcontinent. By the year 2030, over 85 percent of the world's diabetic patients will be in developing countries. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in 2000 to 79.4 million in 2030 [2]. These estimates are valid only if the prevalence of obesity remains the same. Since the incidence of obesity is rising at an alarming rate in developed and developing countries, the projections for the number of diabetes could well be a gross underestimation.

In the past 20 years, the rates of obesity have tripled in developing countries as they have adopted a Western lifestyle involving decreased physical activity and over consumption of cheap, energy dense food. Such lifestyle changes are also affecting children in these countries; the prevalence of overweight among them ranges from 10 to 25% and the prevalence of obesity ranges from 2 to 10%. The relationship between obesity and poverty is complex: being poor in one of the world's poorest countries (i.e. in countries with a per capita gross national product (GNP) of less than $800 per year) is associated with underweight and malnutrition, whereas being poor in a middle – income country (with a per capita GNP of about $3,000 per year) is associated with an increased risk of obesity. A developing country like India, faces the paradox of families, in which the children are underweight and the adults are overweight. This combination has been attributed by some people to intrauterine growth retardation resulting in low birth

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weight, which apparently confers a predisposition to obesity later in life through the acquisition of a "thrifty" phenotype that, when accompanied by rapid childhood weight gain, is conducive to the development of insulin resistance and metabolic syndrome [3].

The Indian Scenario

A national survey of diabetes conducted in six major cities in India in the year 2000 has shown that the prevalence of diabetes in urban Indian adults was 12.1% [4]. The onset of diabetes among Indians is about a decade earlier than their western counterparts and this has been noted in Asian Indians in several studies [5]. In the national survey 54.1% of diabetes developed it in the most productive years of their lives i.e. before the age of 50 years and they also had a higher risk of developing chronic complications of diabetes [5,6]. The prevalence of Type 2 diabetes is 4-6 times higher in the urban areas as compared to rural areas. The prevalence of impaired glucose tolerance (IGT) in the rural population is also high at 7-8%, which indicates presence of a genetic basis for Type 2 diabetes in ethnic Indian population [7].

Risk Factors

Risk factors for developing Type 2 diabetes, peculiar to the Indian population are high familial aggregation, central obesity, insulin resistance and life style changes due to urbanization. In India nearly 75% of the Type 2 diabetics have first degree family history of diabetes indicating a strong familial aggregation [8]. Insulin resistance has been demonstrated to be a characteristic feature of Asian Indians. Comparison of Asian Indians, Europeans and other ethnic groups have shown that the former have higher insulin response than others, at fasting and in response to glucose [9]. Asian Indians require higher levels of plasma insulin to maintain normoglycaemia; they also have other features of insulin resistance such as central obesity and high percentage of body fat in comparison to many other populations [9].There are two studies from India which relate the size at birth or birth weight to future risk of Type 2 diabetes [10,11]. In the study from Mysore, low birth weight did not increase the risk of diabetes but babies who were short and fat at birth were at increased risk [10]. Most investigators have suggested that the rise in Type 2 diabetes in urban population may have been triggered by mild obesity in mothers leading to glucose intolerance during pregnancy, macroscopic changes in the fetus, and insulin deficiency in adult [10-13]. Yajnik et al [12], have reported that high prevalence of Type 2 diabetes and IGT in Indians may be linked to poor fetal growth. There is a possibility that Type 2 diabetes may be programmed in fetal life due to changes in intrauterine milieu interior. This may be due to nutritional deprivation or one of nutritional plenty. It leads to changes in pancreatic development and peripheral response to insulin which may cause gestational diabetes mellitus (GDM) and adult onset Type 2 diabetes. GDM increases the lifetime risk of developing diabetes, at over 3 times compared to controls at 16 years after index pregnancy [14]. By 17 years of age one- third of children born of gestational diabetic mothers have had evidence of IGT or Type 2 diabetes [15]. In an Indian study, one-third of the women who developed GDM had maternal history of diabetes [16].

Obesity also shows familial aggregation among Indian population. Central obesity is common among Indians despite low rates of general obesity and this android pattern of body fat typified by more upper body adiposity measured as waist to hip ratio (WHR) was found to be a greater risk factor as compared to general obesity [5,6,17]. According to World Health Organization (WHO) recommendation a body mass index (BMI) of 18.5-22 kg/m^2 is considered healthy for Asian population [18]. Asian Indians generally have lower BMI than many other races but the association of BMI with glucose intolerance is as strong as in any other population [19]. It was demonstrated that in urban Indian population with a BMI of > 23 kg/m^2, the risk of diabetes is significant for both genders [20]. Asian Indians have higher upper body adiposity measured as WHR. The cut-off values for normal waist circumference were 85 and 80 cm and 0.89 and 0.81 for WHR in men and women respectively [21].

The existence of high insulin resistance despite a lower BMI could be explained by the upper body adiposity present in Asian Indians. Central obesity indicates deposition of large quantities of abdominal fat, which consists of visceral fat and subcutaneous fat. Visceral fat increases the risk of diabetes and hyperlipidemia by favoring insulin resistance. Increased risk posed by intra-abdominal fat for diabetes and other metabolic diseases could be related to higher fat cell number in the abdominal adipose tissue, higher blood flow, increased receptors for cortisol and testosterone and greater catecholamine induced lipolysis when compared with subcutaneous adipose tissue [21]. In addition, there is a marked increase in the influx of non-esterified fatty acids to the liver in abdominally obese subjects. There is sufficient evidence to show that abdominal obesity causes insulin resistance and it is key component of the metabolic syndrome. Racial susceptibility to insulin resistance and metabolic syndrome has been demonstrated and Indians are highly susceptible to both [22]. McKeigue et al [20], reported that in Asian Indians every 0.04 unit increase in WHR was associated with four fold rise in diabetes

(20% in Asians vs 5% in Europeans), two fold higher post glucose insulin levels (41 μU/ml in Asians vs 19 μU/ml in Europeans) and significantly higher triglycerides and low high density lipoprotein.

Urbanization has brought about several changes in the life style in India like consumption of excess calories and reduction in complex carbohydrates with increased consumption of simple sugars and fats. Moreover energy saving methods of transport and labour have resulted in severely reduced physical activity. Sedentary life style is one of the significant factors associated with diabetes in this population. It has also been noted that clustering of the risk factors for cardiovascular disease like hypertension, glucose intolerance, increased two hour insulin, dyslipidemia and obesity occur frequently in urban Indian population [23,24]. In the recently conducted Chennai Urban Population Study (CUPS) by Mohan et al [25], it has been again emphasized that the incidence of diabetes was 20.3 per 1000 person years and that of prediabetes was 13.1 per 1000 person years even among subjects with normal glucose tolerance.

Unfortunately, obesity and diabetes are no longer diseases just of adults. The United States and many other countries have seen a surge in the number of children and adolescents with obesity, insulin resistance and Type 2 diabetes. While Type 2 diabetes previously represented less than 5% of newly diagnosed diabetes in children in the United States, it now represents as much as 45% of the new diagnosis [26]. Similar to adults, this rise in pediatric obesity and diabetes is thought to be largely related to environmental factors including decreased physical activity and increased caloric intake. In a study of school children in New Delhi, 18% were overweight and 27% had impaired glucose tolerance [27]. It is estimated that 15-25% of urban school children in India are at risk of developing Type 2 diabetes at an early age [28].

Complications of Diabetes

Diabetes mellitus basically produces changes in the blood vessels and hence can affect almost every part of the body. Long standing diabetes mellitus is associated with an increased prevalence of micro-vascular and macro-vascular diseases. The onset of Type 2 diabetes is usually insidious and the patient may remain asymptomatic until late stages of the disease. The prevalence of retinopathy is high among the Indian Type 2 diabetic subjects. A study by Mohan et al [23], in South India found it in 34.1% of their patients. Diabetic nephropathy develops in about one third of patients with diabetes and its incidence is sharply increasing in the developing world, with the Asia-Pacific region being the most severely affected. According to a survey published in 2003 [29], diabetic nephropathy was the most common cause of end stage renal disease in 9 of 10 Asian countries, with an incidence that had increased from 1.2% of the overall population with end-stage renal disease in 1998 to 14.1% in 2000. However the prevalence of nephropathy among native Indians was less at 8.9% in Vellore and 5.5% in Chennai, compared to a prevalence of 22.3% among Asian Indians in the UK [30]. The prevalence of nephropathy in the white population was 12.6%. A strong familial clustering of diabetic nephropathy in Indian Type 2 diabetics was also noted [30]. This study also demonstrated that proteinuria was present in 50% and microalbuminuria in 26.7% of the probands with diabetic nephropathy. In a study among 4837 patients with chronic renal failure, the prevalence of diabetic nephropathy was 30.3% followed by chronic interstitial nephritis (23%) and chronic glomerulonephritis (17.7%) [31]. Recent studies have shown that the prevalence of coronary heart disease (CHD) in Indian diabetics may be as high as in the migrant population. The prevalence of CHD, measured as major Q wave changes was 3.9%, almost similar to Asian Indians in UK (4.0%) [24]. The prevalence of peripheral vascular disease (PVD) among Indians is 4-6% which is comparatively lower as compared to 9.3% among the white population [32]. Diabetic foot is a common cause of hospital admissions among diabetics in India. Diabetic neuropathy is also common and an additional risk factor for foot infections [33]. Clustering of cardiovascular risk factors or syndrome X- namely central obesity, general obesity, hyperinsulinemia, dyslipidemia, hypertension and glucose intolerance has been noted in urban Indians in various studies [23,24,34]. The combination of one or more components of syndrome X occurred frequently (1.5 to 4 times) than expected by chance [34].

Screening, Prevention and Treatment

The insidious onset of the disease and long duration of asymptomatic disease before the symptoms develop makes the prevalence of complications quite high even at the time of diagnosis of Type 2 diabetes. The screening tests for complications at the time of diagnosis becomes imperative not only for early detection, but also to prevent progression to end stage diseases. Hence a country like India with its large burden of diabetes and vulnerability to chronic complications, must evolve strategies for primary prevention of diabetes and its complications. Early screening and therapeutic interventions are the first steps towards achieving this goal. Universal screening during pregnancy is very important in our country as Indian women have eleven fold increased risk of developing IGT during pregnancy as compared to Caucasian women [35]. Primary

prevention of diabetes is possible by influencing the environmental factors such as obesity, diet and physical activity. This should start during intrauterine period and continue throughout life from early childhood. It will involve screening of all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition to prevent in all probability, the vicious cycle of transmitting glucose intolerance and/or diabetes from one generation to another [36].

Once diabetes is diagnosed, adequate treatment requires a significant amount of resources for patients i.e. access to glucometers, medications, regular access to health care and referral to specialists for management of complications. For a person of low economic standing in India, diabetes care can account for 25% or more of their family income for each person with diabetes. The management of long-term complications of diabetes is costly and also leads to enormous productivity losses with significant social burden to the patient and family.

Life style changes/interventions and drugs are the current strategies that exist to prevent or reduce the onset of diabetes. The Diabetes Prevention Programme Research Group study found that the lifestyle interventions undertaken over 2.8 years can reduce the incidence of Type 2 diabetes by about 58% [37]. In the Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication (DREAM) trial, subjects over 30 years of age with impaired fasting glucose or impaired glucose tolerance or both with no previous cardiovascular disease were randomized to receive rosiglitazone (8 mg) or ramipril (15 mg) or placebo [38]. It was found that in those receiving rosiglitazone only, 11.6% developed diabetes compared to 26% of those receiving placebo. These results were statistically significant ($p<0.0001$). Ramipril on the other hand did not have any beneficial effect in this study. Though life style changes are effective preventive method, the effects of the same are at times difficult to replicate in different settings. On the other hand providing drugs is expensive and the side effects need careful monitoring. However pragmatic life style interventions can definitely delay and/or prevent diabetes and host of other disorders.

It is beyond doubt that India has the largest number of diabetics in the world and the Government of India has rightly launched the national programme for control of diabetes, cardiovascular diseases and stroke in January 2008 [39]. The responsibility of keeping our present as well as future race free from preventable diseases like diabetes, hypertension and CHD lies on each and every one of us. Hence intervention strategies like "Eat less, Eat on time and Walk more" have to be inculcated to save our children and youth from developing these present day disorders.

Conflicts of Interest

None identified

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