TYPE 2 DIABETES MELLITUS – THE EPIDEMIC OF THE 21ST CENTURY: THE INDIAN SCENARIO

A Ramachandran*, C Snehalatha*

Diabetes mellitus is the commonest metabolic abnormality in the world. Type 2 diabetes (Non-insulin dependent diabetes, NIDDM) is the commonest form of diabetes constituting nearly 90% of the diabetic population in any country. The prevalence of type 2 diabetes varies in different geographic regions and also in different ethnic groups. Prevalence of type 2 diabetes is increasing in most of the countries, especially in developing countries such as India [1]. The first authentic data on the prevalence of diabetes in India came from the multicentric study conducted by the Indian Council of Medical Research (ICMR) in the early seventies. This study reported a prevalence of 2.3% in the urban and 1.5% in the rural areas [2]. The criteria used in this study were different from those set by the WHO expert Committee on Diabetes Mellitus [3].

The interest in the epidemiology of diabetes was sparked off by the reports from several nations such as Fiji, Singapore, Mauritius, Tanzania, South Africa and UK, which showed a high prevalence of type 2 diabetes among migrant Asian Indian populations compared with the host populations and other migrant ethnic groups [4-6] (Table 1). The higher prevalence in Asian Indians was attributed to a high genetic susceptibility to the disease which was unmasked when they migrated to more affluent environments.

Assuming the Indians as an ethnic group have a high degree of genetic predisposition to develop diabetes, one could expect higher prevalence of diabetes among the native urban populations with a comparable affluent life style. In the last two decades, epidemiological studies in several Asian countries including India, have revealed a high prevalence of type 2 diabetes among the urban populations in homeland. Studies in India in the last decade have highlighted that not only prevalence of type 2 diabetes is high, but it is increasing in the urban population (Table 2).

The first study by Diabetes Research Centre, Madras in 1984 [7] was taken up to assess the prevalence of type 2 diabetes and IGT in an urban township, using the WHO criteria. The prevalence of type 2 diabetes was found to be 5%. If environmental factors do have a significant role in the pathogenesis of diabetes, one would expect a lower prevalence in the rural areas where the populations follow a conventional life style. Such an urban-rural difference in the prevalence rate was found in another survey conducted by the Diabetes Research Centre in Madras on two populations belonging to the same ethnic group but with different socio-economic status [8]. The age-adjusted prevalence of diabetes was 8.2% in the urban and 2.4% in the rural populations with 8.4% in urban men and 7.9% in urban women.

Table 1 : Prevalence of diabetes in migrant Indians compared to other ethnic groups

			Prevalence (%)						
Year	Author	Country	Europeans	Africans	Melanesians	Malays	Chinese	Creole	Indians
1983	Zimmet et al	Fiji			7.1 1.2 (U) (R)				11.0 11.3 (U) (R)
1988	McKeigue et al	East London	4.0						23.0
1989	Simmons et al	Coventry, UK	2.8						11.2
1989	Dowso et al	Mauritius					11.5	10.3	12.5
1989	Swai et al	Tanzania		1.9					7.1
1992	Cheah & Thai	Singapore				9.3	8.0		12.8
		Malaysia				3.0	4.9		16.0
1994	Ornar et al	South Africa							13.0

U-Urban R-Rural

*Diabetes Research Centre, 4 Main Road, Royapuram, Chennai, India

Similar urban-rural difference in the prevalence of diabetes in India have been shown in the studies from Orissa and also by the ICMR.

Table 2 : Studies of the prevalence of diabetes mellitus of India

Year	Author	Place	Prevalence(%) Urban	Rural
1971	Tripathy et al	Cuttack	1.2	-
1972	Ahuja et al	New Delhi	2.3	-
1979	Gupta et al	Multicentre	3.0	1.3
1984	Murthy et al	Tenali	4.7	-
1986	Patel	Bhadran	3.8	-
1988	Ramachandran et al	Kudremukh	5.0	-
1989	Kodali et al	Gangavathi	-	2.2
1989	Rao et al	Eluru	-	1.6
1991	Ahuja et al	New Delhi	6.7	-
1992	Ramachandran et al	Madras	8.2	2.4
1997	Ramachandran et al	Madras	11.6	-
1998	Shekhar Shah et al	Assam	8.2	-

A rising trend in the prevalence of diabetes in urban areas was evident in several studies conducted in different parts of India (Table 3).

Table 3 : Prevalence (%) of type 2 diabetes in South East Asia

	Year	Urban	Rural
India	1972	2.3	-
	1979	3.0	1.3
	1988	5.0	-
	1992	8.2	2.4
	1997	11.5	-
Singapore			
Chinese	1984	4.0	-
	1992	8.0	-
Malays	1984	7.6	-
	1992	9.3	-
Migrant Indians	1984	8.9	-
Philippines	1992	8.4-12.0	3.8-9.7
Malaysia	1984	3.3	-
	1988	6.6	-
	1994	12.2	-
Thailand	1971	2.5	-
	1986	6.0	6.0
	1989	6.7	-
Vietnam		2.5	1.4
Srilanka	1994	-	5.0
	1995	8.1	-

An increasing prevalence of diabetes is seen in many countries [4-6]. Prevalence of diabetes and IGT are high in reports published from Pakistan (16.2% of men and 11.7% of women have diabetes and 9% have impaired glucose tolerance). Studies in Singapore have also shown that the prevalence of type 2 diabetes is increasing in all ethnic groups, but the highest increase is seen in the Indians (Table 4) [9].

Table 4 : Rising prevalence of type 2 diabetes Singapore – [Cheah & Thai, 1992]

	1975	1984	1992	%Increase
Total	1.99%	4.7%	8.6%	83
Chinese		4.0%	8.0%	100
Indians		8.9%	12.8%	44
Malays		7.6%	9.3%	22

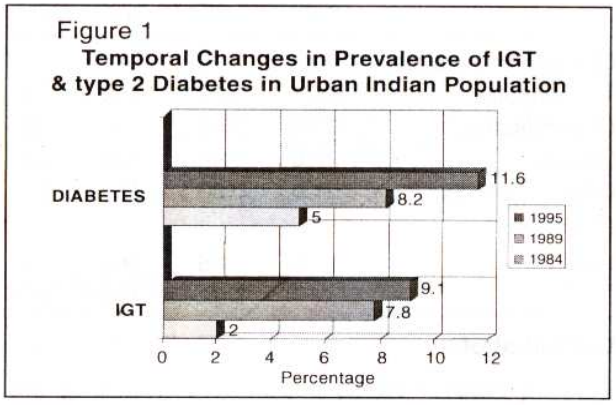
Highest Prevalence in Indians

In UK, Simmons et al [10] reported a high prevalence of type 2 diabetes among various communities that have migrated to UK from northern India and Pakistan, in spite of differences in dietary, cultural and socio-economic factors, thus highlighting the importance of a genetic predisposition to diabetes in these people. In rural areas in India, Bangladesh and other Asian countries, the prevalence of type 2 diabetes is generally lower than that in the urban areas. For example, in urban India the prevalence of type 2 diabetes is 4-6 times higher than in rural areas. However, the number of people with IGT is high (7-8%) even in the rural population, which may indicate the presence of a genetic basis for type 2 diabetes in the ethnic group [8].

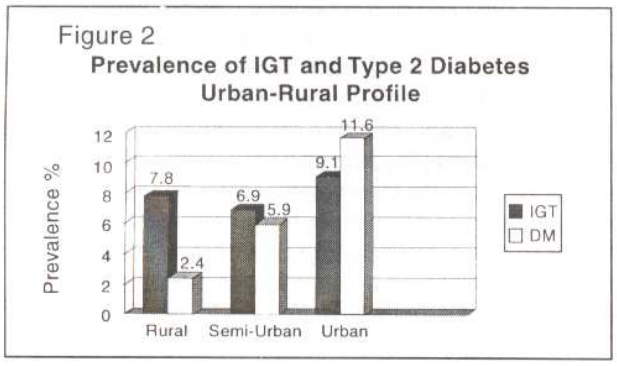
A high prevalence of IGT has been reported in several recent epidemiological studies in developing nations such as India, Pakistan, Bangladesh, South Korea, urban South Africa (7-8%) and other parts of Africa. With increasing urbanization, the conversion rate of IGT to diabetes will increase, and consequently, the prevalence of diabetes [11].

Increasing age is associated with high risk of diabetes. A study of the elderly population, age $\geq$ 60 years, highlighted the high prevalence of diabetes and IGT, with increasing age [12]. Prevalence of diabetes in the urban and rural elderly population were 24% and 9.9% respectively. IGT was detected in 12.4% of the urban and 14.9% of the rural subjects. In another cross sectional study of the temporal changes in the prevalence of type 2 diabetes in urban South India, a 40% increase in the prevalence was noted over a period of 6 years [13].

The prevalence increased from 8.2% in 1988-1989 to 11.6% in 1994-1995 (Figure 1). The age structure of the population studied had not changed significantly, according to the 1991 census. The ratio of newly diagnosed to known diabetes was 1:3 in the urban and 1:1 in the rural areas. We studied the effect of urbanization on the prevalence of diabetes and IGT in the South Indian population by choosing a rural population living on the outskirts of the city.



Prevalence of diabetes was found to be 5.9% in this population which was intermediate to that in the urban (11.6%) and rural (2.4%) population [14]. Although majority of the people were still engaged in manual labour, more amenities in the form of household equipments, easy accessibility of water and day to day requirements had become available. Prevalence of diabetes in this population was 5.9%, more than two fold higher in comparison with the rural population. Decreasing physical activity was the major determinant of the rising prevalence of diabetes in the semi urban population, in comparison with the urban and rural populations. It is likely that the effect of physical activity is most markedly seen in persons in transitional stage of life style.



This study suggested that sedentary lifestyle may be an important determinant of the increasing prevalence of diabetes in an urbanising population. Prevalence of IGT was high (6.9%) and similar in all three populations we had studied (Figure 2).

Several studied including ours, have shown that type 2 diabetes can remain asymptomatic and undiagnosed for periods upto 4-7 years [15, 16]. During this latent period vascular complications of diabetes such as retinopathy may develop.

Our epidemiological studies have brought into focus that the prevalence of diabetes in urban India is comparable to that in migrant Indian and also that there are similarities in the associated risk factors. Family history of diabetes, age, body mass index (BMI) and waist: hip ratios showed positive association with diabetes in both populations. Despite the low BMI in the rural population, upper body adiposity and BMI were positive risk factors in this relatively non-obese population. The cut off value for BMI for obesity was found to be 25 kg/m^2 in our population.

Familial aggregation

A genetic predisposition to type 2 diabetes is evident from the high familial aggregation of the disease. Asian Indians have strong familial aggregation of diabetes with high prevalence of diabetes among the first degree relatives and vertical transmission through two or more generations. It was found that 45% of the Indians compared to 38% of the Europeans have positive family history of diabetes. An analysis of family history in the type 2 diabetes patients attending the Diabetes Research Centre, Madras, India showed that 54% of the probands had a parent with known diabetes and in an additional 22.8% siblings had diabetes. The prevalence of diabetes increased with increasing family history of diabetes [17]. It was noted that the prevalence of diabetes among offspring with one diabetic parent was 36% which increased to 54% with positive family history of diabetes on the non-diabetic parental side also. The prevalence rate (62%) and risk (73%) increased further when both parents had diabetes.

Insulin resistance

Insulin resistance and beta cell deficiency are the two major pathogenic factors in diabetes. Several studies suggest that insulin resistance is the primary event that leads to abnormalities in glucose metabolism and is present much before the metabolic abnormalities are manifested [18]. When comparing Asian Indians, Europeans and other ethnic groups, researchers have shown that the former have higher insulin response at fasting and in

response to glucose [19]. Our study in the population showed that normoglycaemic Indians had hyperinsulinaemic responses, when compared with the reported values in Europids [13]. Urban-rural differences in plasma insulin responses were seen which might be explained by the differences in the body mass index, diet and physical activity levels [20]. With the availability of more specific assay procedures for specific insulin and proinsulin, it has also been shown that hyperinsulinaemia in Indians is due to higher concentrations of true (specific) insulin [21].

In a prospective study of the offspring, with both parents having type 2 diabetes it was shown that the non obese offspring, who developed diabetes had higher basal insulin response compared to those who remained normoglycaemic [22, 23]. It was thus indicated that insulin resistance may precede the development of hyperglycaemia.

Obesity and central adiposity

Obesity

The relation ship between obesity and type 2 diabetes is complex and is confounded by many heterogenous factors.

Table 5 : Comparison of BMI and WHR in Asian Indians (AI) and Mexican Americans (MA)

	BMI		WHR	
	AI	MA	AI	MA
	Mean ± SD			
Non diabetic	22.1 ± 4.3	27.8 ± 5.2*	0.91 ± 0.07	0.92 ± 0.07
Glucose Intolerant	23.0 ± 4.3	31.0 ± 6.0*	0.96 ± 0.06	0.98 ± 0.06

* Significant
Differences in BMI were significant
Differences in WHR were non significant
Ramachandran et al, DRCP 1997

In all the studies in Southern Indians, BMI has been strongly associated with glucose intolerance, although the mean BMI has been much below the obesity level, both in the urban and rural populations. This suggested that increase in body weight, although within the ideal levels of body mass, could still confer risk of diabetes. The cut off values for ideal body weight applicable to western populations might not hold good in the generally lean Asian Indians. Moreover, insulin resistance which was found to be a characteristic feature of the Asian Indians, despite their lean body mass, could be adversely affected by even small increments in the body mass. In otherwords higher BMI, rather than obesity seems to be a risk factor in Indians.

Table 6 : Prevalence of Cardiovascular risk factors in urban Indians
Age ≥ 40 years

	Prevalence in %	O/E Ratio		
	Total	Isolated	Combination +1	Combination +2
Glucose Intolerance	39.1	0.29	3.7	1.5
↑ 2h Insulin	55.1	0.77	2.9	1.0
Dyslipidaemia	50.8	0.65	2.4	1.3
Obesity	27.0	0.44	4.0	1.7
Central Obesity (↑ WHR)	61.0	0.83	2.5	1.2
HTN	21.8	1.5	3.8	1.4

Diabetes Care, 1998

Central Obesity

In several ethnic populations including the relatively non-obese South Indian population, the android pattern of body fat, typified by more upper body adiposity, measured as waist hip ratio (WHR), was found to be a greater risk factor for type 2 diabetes than general obesity [13, 9, 24]. Our study has shown that southern Indians who have a low rate of obesity have high WHR, indicating that central obesity is common despite low rates of obesity. This has been found to be true of other Indian populations also. Indians with low BMI have WHR comparable to the Mexican Americans, (Table 5) who are obese [25]. The risks conferred by increasing BMI and WHR are high in both populations when compared with the white population.

Clustering of risk factors

A population study conducted in urban South India, by the Diabetes Research Centre, showed that there was a high prevalence of the clustering of cardiovascular risk factors namely, central adiposity, obesity, hyperinsulinaemia, dyslipidaemia, hypertension and glucose intolerance in the adults aged ≥ 40 years [26]. Isolated prevalence of individual components were lower and combinations of one or more of them occurred more frequently (1.5 to 4 times) than expected by chance (Table 6). The clustering of these risk factors have been described both in cross sectional and prospective studies in the Europeans. This was originally described by Reaven and referred to as syndrome 'X' [27]. Our study had shown the

prevalence of syndrome 'X' in urban Indians, for the first time. In this study, the prevalence of probable CHD in the adult Indians was found to be 3.9%. This figure was similar to the prevalence reported in migrant Indians in UK [28]. An additional 10% had T wave inversion, suggestive of possible CHD. An interesting observation made in this study was that hypertension was not associated with hyperinsulinaemia in Indians.

Magnitude of the problem

At present, it is calculated that there is about 20-25 million people with diabetes in India and by the year 2000 it is likely to increase to 30-35 million (Table 7). In other words, India will have the largest number of diabetic subjects in the world and one out of every four diabetic subject in the world will be an Indian.

Table 7 : Estimated burden of diabetes in India Adults ≥ 20 years

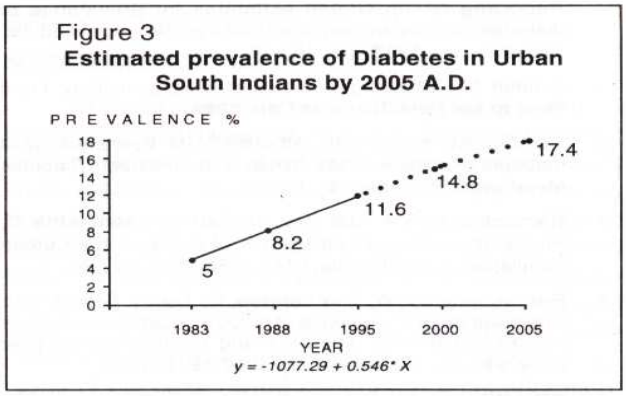
	Year		
	1990	1995	2000
NIDDM %			
Urban	8.2	11.6	14.7
Rural	2.4	2.4	2.4
Number Diabetic (Millions)	22	28	33

The report by the WHO ad hoc diabetes reporting group published in 1993, showed that the burden of diabetes will be maximum in the developing countries, like India [4]. The report published in 1998 supported the earlier predictions of the epidemic nature of diabetes in the world during the first quarter of the 21st century [5]. It was estimated that the prevalence of diabetes in the world would increase from 4% in 1995 to 5.4% in the year 2025. The major part of the numerical increase will occur in developing countries. There will be a 42% increase from 51-72 million in the developed countries and 170% increase from 84-228 million, in the developing countries (Table 8). The countries with largest number of diabetic people are, and will be in the year 2025, India, China and United States. In developing countries, the diabetic subjects would be younger, 45-64 years of age, and in the developed countries majority of the diabetic subjects would be aged ≥ 65 years (Table 8).

Table 8 : Prevalence, numerical estimates and Projections of diabetes King et al 1998

	World		Developed Countries		Developing Countries	
	1995	2025	1995	2925	1995	2025
Diabetes Prevalence %	4.0	5.4	6.0	7.6	3.3	4.9
% Increase	35		27		48	
Number million	135	300	51	72	84	228
% increase	122		42		170	
↑ adult population %	60		11		80	
Number in billions	>5		~1		>4	

Based on the data from our serial studies, it has been predicted that the prevalence of diabetes will become 14.7% in 2000 A.D. and 17.4% in 2005 A.D. (Figure 3).



These figures project not only the magnitude of the burden of diabetes in India and other developing countries but also show that it would affect the middle aged population, in the peak of their lives. Therefore, there is an urgent need to take up steps to identify the potential diabetic subjects and to implement primary strategies to reduce the risk of diabetes in the population.

Serial epidemiological studies conducted by the Diabetic Research Centre, Madras and also the studies in migrant Indian population showed that the major risk factor for the rising prevalence of type 2 diabetes are:

1. Genetic predisposition
2. Insulin resistance
3. Obesity
4. Central Obesity
5. Urbanisation with change in diet habit and sedentary life style.

Except for the first factor, the other risk factors can be modified by life style changes involving dietary modifications and improved physical activity. These life style modifications have been shown to improve the glucose tolerance thereby preventing or

delaying the onset of diabetes in individuals genetically-prone to develop the disorder [29-32].

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