Burden of type 2 diabetes and its complications – The Indian scenario

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India faces a grave health care burden due to the high prevalence of type 2 diabetes and its sequalae. Epidemiological data from different parts of the country show a rising prevalence of diabetes in the urban areas. A national study in 2000 AD showed that the prevalence in urban adults aged ≥ 20 years was 12.1%. Onset of diabetes occurs at a younger age in Indians, giving ample time for development of the chronic vascular complications. Moreover, impaired glucose tolerance (IGT), which is a forerunner of diabetes, is also increasing, especially among the younger population. There is a wide urban–rural difference in the prevalence of diabetes indicating a major role for urbanization in the causation of the disease. Indians are also susceptible to the major complications related to diabetes like coronary artery disease, neuropathy, nephropathy and retinopathy. Prevalence of the complications is higher in low socio-economic groups due to lack of good control of glycaemia and hypertension and also due to behavioural factors. The direct and indirect costs involved in the treatment of the chronic disease especially when associated with the vascular complications are enormous. There is an urgent need to implement preventive measures to reduce the high morbidity and mortality and also to reduce the cost burden to the patients and to the society.

Global prevalence of diabetes

TYPE 2 diabetes is the commonest form of diabetes constituting 90% of the diabetic population. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025 (ref. 1). The World Health Organization has predicted that the major burden will occur in the developing countries. There will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million, in the developing countries. The countries with the largest number of diabetic people are, and will be in the year 2025, India, China and United States[1].

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Diabetes in Indians

Epidemiological studies among migrant Asian Indians in many countries showed higher prevalence of type 2 diabetes compared with the host populations and other migrant ethnic groups[2] (Table 1). Studies conducted in India in the last decade have highlighted that not only is the prevalence of type 2 diabetes high, but also that it is increasing rapidly in the urban population[3–7] (Table 2). Three diabetic surveys conducted in Chennai in years 1989 (ref. 8), 1995 (ref. 9) and 2000 (ref. 10) were compared for the age – standardized prevalence, anthropometric, demographic and lifestyle characteristics of the glucose intolerant groups. A rising trend was statistically significant for diabetes (χ^2 = 18.0, $P < 0.001$) and for impaired glucose tolerance (IGT) (χ^2 = 48.2, $P < 0.001$) (Figure 1). The period between 1989 and 1995 showed a 40% rise in the prevalence and subsequently a further increase of 16.4% was seen in the next 5 years. A national survey of diabetes conducted in six major cities in India in the year 2000 showed that the prevalence of diabetes in urban adults was 12.1%. Prevalence of IGT was also high (14.0%) (ref. 10). A younger age at onset of diabetes had been noted in Asian Indians in several studies[10,11]. In the national study, onset of diabetes occurred before the age of 50 years in 54.1% of cases, implying that these subjects developed diabetes in the most productive years of their life and had a greater chance of developing the chronic complications of diabetes.

Urban–rural difference

An urban–rural difference in the prevalence rate was found indicating that the environmental factors related to urbanization had a significant role in increasing the prevalence of diabetes[8]. The prevalence of diabetes in urbanizing rural population was found to be midway between the rural and urban populations[12] (Figure 2).

Significance of impaired glucose tolerance

A startling increase in the prevalence of IGT was observed between 1995 and 2000 AD, especially among the young urban population below the age of 40 years (Figure 3).

Table 1. Prevalence of diabetes in migrant Indians compared to other ethnic groups[2]

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

Table 2. Studies showing a rising trend in the prevalence of Type 2 diabetes in India

				Prevalence (%)	
Year	Author	Place	Area	Urban	Rural
1971	Tripathy *et al.*	Cuttack	(Central)	1.2	
1972	Ahuja *et al.*	New Delhi	(North)	2.3	
1979	Gupta *et al.*	Multicentre		3.0	1.3
1984	Murthy *et al.*	Tenali	(South)	4.7	
1986	Patel	Bhadran	(West)	3.8	
1988	Ramachandran *et al.*	Kudremukh	(South)	5.0	
1989	Kodali *et al.*	Gangavathi	(South)		2.2
1989	Rao *et al.*	Eluru	(South)		1.6
1991	Ahuja *et al.*	New Delhi	(North)	6.7	
1992	Ramachandran *et al.*	Madras	(South)	8.2	2.4
1997	Ramachandran *et al.*	Madras	(South)	11.6	
2000	Ramachandran *et al.* (DESI)	National Urban		12.1	
2001	Ramankutty *et al.*	Kerala		12.4	2.5

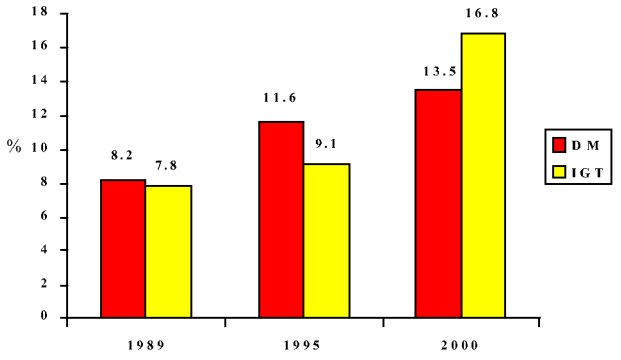

Figure 1. Increasing prevalence of diabetes and IGT in south India.

With the estimate that nearly one third of the IGT population develop diabetes eventually[13], the observation is suggestive of a potential increase in diabetes in the coming years. IGT being a condition associated with severe insulin resistance, the metabolic abnormalities, which tend to cluster with IGT and insulin resistance could lead to a rise in cardiovascular diseases also[14]. IGT is a known risk factor for diabetes and coronary heart disease[15].

Although the prevalence of Type 2 diabetes is 4–6 times higher in urban population of India than in the rural areas, 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].

Risk factors

The important risk factors for the high prevalence of diabetes include: (1) High familial aggregation, (2) Obesity especially central obesity, (3) Insulin resistance, (4) Life style changes due to urbanization.

Familial aggregation

Several studies in India and abroad have shown that Indians have a genetic predisposition to diabetes, which gets easily unmasked when the environmental conditions are adverse. The fact that nearly 75% of the type 2 diabetic patients have first degree family history of diabetes indicate a strong familial aggregation in the Indian diabetic patients[16].

Insulin resistance

Insulin resistance has been demonstrated to be a characteristic feature of Asian Indians. Comparison of Asian Indians, Europeans and other ethnic groups has shown that the former have higher insulin response than others, at fasting and in response to glucose[17,18]. Our study in the normoglycaemic urban population showed that they had hyperinsulinaemic responses, when compared with the reported values in Europids[9]. It has also been noted that a clustering of the risk factors for cardio-vascular diseases (CVD) occurs in urban Indian population[3,19] (Table 3).

Obesity also shows a familial aggregation[20]. In all the studies in Indian population, body mass index (BMI) has been strongly associated with glucose intolerance although the mean BMI is much below the obesity level. Insulin resistance gets adversely affected by even small increments in the BMI.

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[8–10,21]. Our studies have shown that central obesity is common in Indians despite low rates of obesity. The adverse effect of central obesity is manifested in increasing tertiles of BMI

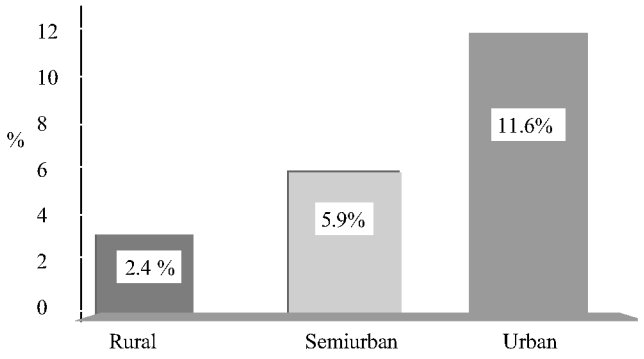

Figure 2. Prevalence of diabetes in different habitats.

Table 3. Clustering of risk factors

	Percentages			
	+1 Other factor		+2 Other factors	
	Obs.	Exp.	Obs.	Exp.
Hypertension	9.2–16.7	4.4	4.7–11.2	8.3
Glucose intolerance	10.2–28.7	7.7	4.7–20.2	13.3
Increased 2 h insulin	16.7–37.3	12.7	7.4–20.1	19.6
Dyslipidaemia	14.5–39.3	16	6.1–25.5	20.1
Obesity	9.2–20.7	5.2	4.7–19.5	11.4

both in men and women, the effect being more evident in women. This is probably one of the reasons for a higher prevalence of diabetes in women in urban area. Indians with low BMI have WHR comparable to the Mexican Americans, who are obese[22]. The risks conferred by increasing BMI and WHR are high in both populations when compared to the white population.

Distribution of body fat

Central adiposity indicates deposition of large quantities of abdominal fat, which consists of visceral fat and subcutaneous fat. Visceral fat increases the risk of diabetes and hyperlipidaemia by favouring insulin resistance.

Our studies in nondiabetic south Indians by measuring the visceral and subcutaneous abdominal fat areas by CAT scan had shown that insulin resistance was associated with subcutaneous fat also, thereby indicating that the subcutaneous fat was not innocuous as had been considered till now[23].

Genetic studies in south Indian subjects showed that an uncoupling protein 2 gene variant (UCP2) was associated with a raised BMI, although it was not related to type 2 diabetes[24]. Such an association was not found in obese British subjects. This gene association may affect the susceptibility to weight gain in Indians when exposed to adverse events[24].

As mentioned earlier, three serial surveys in Chennai showed an increasing trend in prevalence of diabetes and IGT. The risk associations were analysed[25]. Age increased significantly in each survey in both genders. Waist girth and WHR were significantly higher in women, in the 2000 AD survey. There was no significant change in the mean obesity with time in both genders. An increase in IGT was seen in year 2000, especially so in subjects aged < 40 years. Generally the population has lower BMI, much below the cut-off values for obesity level for western population. However, the strong association between the BMI and diabetes indicated that even minor changes in BMI had adverse effects in the population. There had been an increase in the waist circumference and the waist-to-hip ratio only in women over the years. Waist-to-hip ratio is strongly associated with insulin resistance and diabetes and this might explain a shift towards female predominance in the prevalence of diabetes in the population.

The rise in abdominal obesity may be related to the low physical activity in women. Physical activity has been uniformly low in women and in men the percentage with moderate to heavy physical activity reduced by half in 2000 AD[10,25].

Effect of urbanization

Urbanization has brought several changes in the life style in most urban areas in India. These changes include con-

sumption of excess calories, reduction in complex carbohydrates with increased consumption of simple sugars and fats. Such diets have been partly responsible for several diseases including diabetes, cardio-vascular diseases, cancer and gastro-intestinal problems. Moreover availability of energy-saving methods of transport and labour have resulted in severely reduced physical activity. A recent population study in Chennai showed that the total activity level considering the activity at work and during leisure time was very low, especially in women[25]. The activity score was inversely related to the affluence or wealth score and low activity score showed adverse effects on glucose intolerance. The affluence was calculated using a wealth score system and a significant correlation was seen between increasing wealth score and decreasing total activity. Sedentary life style was one of the significant factors associated with diabetes in this population.

Socio-economic influences

Socioeconomic environment influences occupation, life style, and nutrition of social classes which in turn would influence the prevalence and profile of glucose intolerance and diabetic complications. A number of studies have addressed this issue in western countries[26–30]. In urban India, there are wide social and economic disparities. Free health care facilities are available for the economically backward classes, but due to the low level of education and occupational problems, the facilities are not always used.

Prevalence of diabetes was found to be lower in the low socio-economic group living in urban areas compared with the high-income group (12.6 vs 24.6% in subjects ≥ 40 years)[31]. This was probably related to the physical activity of the low income group (LIG) as most of them were involved in moderate to strenuous physical activity at work. Prevalence of diabetes and IGT were significantly lower in the LIG than in the high income group (HIG). The finding of lower prevalence of diabetes in the socially deprived urban Indians was in contrast to the positive association of diabetes and social deprivation in western countries[26–30,32]. However due to inadequate control of diabetes, the long-term complications such as coronary artery diseases were higher in the low socio-economic group. This was to some extent related to the higher rates of risk factors such as uncontrolled diabetes, high cholesterol, hypertension, smoking and alcohol consumption. Factors other than those studied could also have had influenced the increased rates of complications. There was yet another interesting observation that despite having a lower BMI, the low income group had a WHR comparable to the high income group. This probably was an indication that there was a preferential abdominal adiposity in Indians irrespective of the degree of general adiposity.

Mohan *et al.*[3] also found a lower prevalence of diabetes in the LIG compared with middle income group (MIG) in southern India. In another study of the socially-deprived urban slum dwellers, in New Delhi, Misra *et al.* also observed appreciable prevalence of obesity, dyslipidaemia, diabetes (10.3%) and increased body fat in the population. High WHR was observed, especially in women (51.1 vs 9.4% in men) in the study[5].

Diabetic complications

Long-standing diabetes mellitus is associated with an increased prevalence of microvascular and macrovascular diseases. With the rising prevalence of diabetes, the number suffering from the vascular complications of diabetes will also increase.

Table 4 shows the prevalence of the vascular complications observed in a study by the Diabetes Research Centre[33]. Prevalence of retinopathy is high among the Indian type 2 diabetic subjects. A study by Mohan *et al.*[34] in South India showed a prevalence of 34.1% of retinopathy.

The prevalence of nephropathy in India was less (8.9% in Vellore[35], 5.5% in Chennai[33]) when compared with the prevalence of 22.3% in Asian Indians in the UK in the

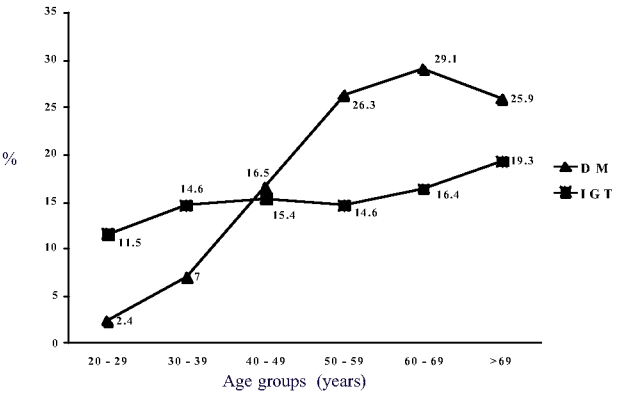

Figure 3. Age-specific prevalence of IGT and diabetes in urban Indian population. Prevalence of IGT was significantly higher than diabetes in the age group below 40 yrs. IGT was 13%, diabetes 5%. $\chi^2 = 206.9, P < 0.0001$.

Table 4. Vascular complications in Type 2 diabetes ($n = 3010$)

Prevalence %			
Complications			
Microvascular		*Macrovascular*	
Retinopathy	23.7	Cardiovascular disease	11.4
Background	20.0	Peripheral vascular disease	4.0
Proliferative	3.7	Cerebro vascular accidents	0.9
Nephropathy	5.5	Hypertension	38.0
Peri-neuropathy	27.5		

study by Samanta *et al.*[36]. The prevalence of nephropathy in the white population was 12.6%.

It is well known that like type 2 diabetes, its vascular complications also have a strong genetic component[37]. A strong familial clustering of diabetic nephropathy in Indian type 2 diabetic patients was noted[38]. The study showed that proteinuria was present in 50% and microalbuminuria in 26.7% of the siblings of probands with diabetic nephropathy. In contrast, the prevalence of proteinuria and microalbuminuria among the siblings of probands with normoalbuminuria was 0% and 3.3% respectively. It was estimated that the incidence of renal failure among the south Indian diabetic patients was 0.69% per annum (CI 0.28–1%) (ref. 39). Diabetic nephropathy is one of the leading causes of chronic renal failure in India. Among 4837 patients with chronic renal failure seen over a period of 10 years, the prevalence of diabetic nephropathy was 30.3% followed by chronic interstitial nephritis (23%) and chronic glomerulonephritis (17.7%) (ref. 40).

A positive association between the *D* allele (*ID* and *DD* genotype) of *ACE* gene polymorphism and diabetic proteinuria in south Indian type 2 diabetic patients was observed[41] which was in agreement with studies in other countries showing such an association. A study had indicated that the risk of CVD was 3-fold higher in nephropathy group than in the nonproteinuric subjects (39 vs 13.2% $P < 0.001$)[42].

Recent studies in India show that the prevalence of CHD in Indians may be as high as in the migrant Indians[19].The prevalence of CHD indicated by major Q wave changes was found to be 3.9% (ref. 19) which was similar to the prevalence in the Asian Indians in UK (4.0%) as shown by McKeigue *et al.*[18]. Another 10.3% had other abnormal ECG changes. A similar prevalence of major Q waves changes was shown by studies in Northern India by Chadha *et al.*[43] (3.2%) and Guptha *et al.*[44] (2.8%).

Prevalence of PVD in Asian Indians is comparatively low compared with the white population (9.3%). Low prevalences of PVD were demonstrated in Indian patients by Mohan *et al.*[45] (overall 3.2%, 6.3% in diabetes) and also in our study (4.0%) (ref. 33).

Diabetic foot infections are a major problem and a common cause for hospital admission of diabetic patients in India. Although the prevalence of PVD is low, neuropathy is very common and is an associated risk factor for foot infections, which often tend to recur[46].

Clustering of cardiovascular risk factors

Clustering of cardiovascular risk factors (or syndrome 'X') namely central adiposity, obesity, hyperinsulinaemia, dyslipidaemia, hypertension and glucose intolerance has been noted in urban Indians in studies by Ramachandran *et al.*[19] by Mohan *et al.*[3] and by Mishra *et al.*[47]. Isolated prevalence of individual components was lower and combinations of one or more occurred more frequently (1.5–4 times) than expected by chance[19] (Table 3).

India is going to face a big challenge posed by the rising prevalence of diabetes and its complications unless steps are taken to implement the primary and secondary prevention in diabetes. For this purpose it is essential to identify the risk factors for diabetes and also for the vascular complications.

Two landmark studies, the United Kingdom Prospective Diabetes Study (UKPDS) in type 2 diabetes[48] and the Diabetes Control and Complications Trial in type 1 diabetes[49] have shown that tight control of hyperglycaemia and hypertension could reduce the risk of vascular complications to a great extent. Early diagnosis of diabetes and control of hyperglycaemia and hypertension will help in secondary prevention in diabetes.

Primary prevention of diabetes is possible by modifying the environmental factors influencing diabetogenesis such as obesity, diet and physical activity. Long-term studies have shown the beneficial effects of life-style modifications on reducing the risk of diabetes[50–52].

India needs to implement the preventive measures to reduce the burden of diabetes as it poses a medical challenge which is not matched by the budget allocations for diabetes care in India. It is estimated that the annual cost of diabetes care would be approximately 90,200 million rupees. The average expenditure per patient per year would be a minimum of Rs 4,500 (ref. 53).

Type 1 diabetic patients and patients with complications face additional economic burden. Among the type 1 diabetic patients, fifty six percent of patients were not earning. The median percentage of income spent on diabetes was 22% for the entire group, varying from 59% in the low socioeconomic group, 32% in the middle socioeconomic group, 18% in the upper middle income group and 12% in the high income group. Patients managed on an outpatient basis incurred an expenditure of 16% of income while 23% of income was spent on those requiring hospitalization[54].

We found that diabetic patients without complications like foot problems spent Rs 4373, which was similar to the above report. The expenditure on care of foot problems increased significantly, outpatient care requiring a median of Rs 7200 and in-patient care requiring Rs 16,910 in a year. This assumes great importance because foot complications are a major cause for hospitalization cost and morbidity and most of them are preventable[55]. There is an urgent need to implement preventive measures to reduce the cost of the disease, which involves direct and indirect costs to the patient and to the society also.

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