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1 - EPIDEMIOLOGY OF DIABETES IN DIFFERENT REGIONS OF INDIA

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ABSTRACT

India is currently experiencing an epidemic of diabetes mellitus. In order to understand the true extent of the problem and its impact on diabetes care, there is a need to review the epidemiology of diabetes from different regions of India. Epidemiology of diabetes in India has an extensive history. The earliest national study reported an overall prevalence of 2.1 % in urban areas and 1.5% in rural areas. From the available region wise population based studies it is clear that in the last two decades, there has been a marked increase in the prevalence of diabetes among both urban as well as the rural Indians, with southern India having the sharpest increase. Subsequent studies confirmed this high prevalence of diabetes in urban south India. Today, the prevalence of diabetes in the urban metros of India is approaching the figures reported in the affluent migrant Indians. Although in rural India the prevalence of diabetes is much lower than in the urban population, even here the prevalence of diabetes is rapidly rising, though clearly more studies are needed. Nevertheless, there is enough information to derive significant conclusions and projections that will not only help define the burden of diabetes in India but also throw some light on the causes of the diabetes epidemic. Environmental and lifestyle changes resulting from industrialization and migration to urban environment from rural settings may be responsible to a large extent, for this epidemic of Type 2 diabetes in Indians. In addition, given the large number of people with Type 2 diabetes in our country, the morbidity due complications associated with it would still be very high. Thus, effective preventive programmes need to be urgently implemented to stem the tide.

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Diabetes is fast becoming the epidemic of the 21st century. Type 2 diabetes, which is more prevalent (more than 90% of all diabetes cases) and the main driver of the diabetes epidemic, now affects 5.9% of the world's adult population with almost 80% of the total in developing countries [1]. Nowhere is the diabetes epidemic more pronounced than in India as the World Health Organization (WHO) reports show that 32 million people had diabetes in the year 2000 [2]. The International Diabetes Federation (IDF) estimates the totaj number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [1].

Epidemiology of diabetes in India has an extensive history. To do a comparative analysis on the epidemiology of prevalence of diabetes in the first half of 20th century is difficult as there were no standard criteria for diagnosing diabetes. Most of the earlier studies conducted in the early and mid-20th century were based on hospital and clinic records and used glycosuria as the diagnostic criteria. The earliest documented study on prevalence of diabetes in India was done in Calcutta (now Kolkata) in 1938 [3]. Out of the 96,300 medical records checked, 1% was found to have diabetes diagnosed by glycosuria. In Bombay (now Mumbai) reports on test for detection of diabetes in large number of subjects were first available in 1959 [4]. Following this, several groups of scientists in other parts of the country carried out similar detection programmes in 1966 [5-8]. Subjects screened were from large gatherings for other purposes or those who volunteered for the tests at detection camps. There was neither systematic sampling nor efforts for testing the total population of a limited area.

Early in the 1970's a systematic collaborative study on diabetes in 6 different parts of the country was conducted by the Indian Council of Medical Research (ICMR). This multicentric study conducted between 1972 and 1975 [9] in 34,194 individuals [19077- urban and 15117—rural] aged above 15 years used uniform methodology and sampling techniques. Population sampling was based on a stratified, random design in urban areas and on cluster sampling in rural areas. Capillary blood glucose was used for diagnosis of diabetes. This study reported an overall prevalence of 2.1 % in urban areas and 1.5% in rural areas, while in those above 40 years of age, the prevalence was 5% in urban and 2.8% in rural areas [9]. **Figure 1** shows the prevalence of type 2 diabetes in urban and rural areas in different parts of India [9].

Another population based study - National Urban Diabetes Survey (NUDS) was conducted in six large cities from different regions of India in 2001. This study was done on 11,216 subjects aged over 20 years from all socio-economic strata [10]. The WHO criterion was used for diagnosis diabetes after an Oral Glucose Tolerance Test using capillary blood. The study showed that the age standardized prevalence of type 2 diabetes was 12.1%. The prevalence was the highest in Hyderabad (16.6%), followed by Chennai (13.5%), Bengaluru (12.4%), Kolkatta (11.7%), New Delhi (11.6%) and Mumbai (9.3%). The NUDS results also indicate that the prevalence of impaired glucose tolerance (IGT) was higher than that of type 2 diabetes in four out of six cities studied (80). The prevalence of IGT was 16.8% in Chennai, 14.9% in Bengaluru (formerly Bangalore), 29.8% in Hyderabad, 10% in Kolkatta, 10.8% in Mumbai and 8.6% in New Delhi [10]. Today, the prevalence of diabetes in the urban metros of India is approaching the figures reported in the affluent migrant Indians.

The Prevalence of Diabetes in India Study (PODIS) was carried out in 108 centres (49 urban and 59 rural) in different parts of India to look at the urban-rural differences in type 2 diabetes and glucose intolerance in the year 2004 [11,12].

Diabetes was defined according to WHO and ADA criteria. According to ADA criteria, the prevalence of diabetes was 4.7% in the urban and 1.9% in the rural areas. The prevalence of diabetes according to WHO criteria was 5.6% and 2.7% among urban and rural areas respectively. Recently The Sentinel Surveillance Systems for cardiovascular disease (CVD) was carried out in Indian industrial populations [13], in ten centres from different parts of the country (n=19,973 subjects for the questionnaire survey, n = 10,442 for biochemical investigations). This study documented prevalence of diabetes to be 10.1 % using ADA criteria and the prevalence of self reported diabetes was 5.6% in this study population.

Recently a national NCD risk factor surveillance [14] was conducted in six different geographical locations (East, South, North, West/ Central India) in India. There was a geographical difference in the overall prevalence of self-reported diabetes, with the centres in southern states having a higher prevalence [Trivandrum (9.2%); Chennai (6.4%)] compared with north [Delhi (6.0%); Ballabgarh (2.7%)], east [Dibrugargh (2.4%)] and west/central India [Nagpur (1.5%)]. Similar trends were observed even when categorized based on residential areas as urban, periurban/slum and rural areas, except for urban areas where Delhi had higher rates (10.3%) than Chennai (8.7%) and Dibrugarh (5.5%) had higher rates than Ballabgarh (4.8%) **[Figure 2]**. This study showed that the lowest prevalence of self-reported diabetes was recorded in rural (3.1%) followed by peri-urban/slum with 3.2% and the highest prevalence was observed in urban areas (7.3%).

From these national reports, it is evident that till the 1970s, the prevalence of diabetes was less than 3.0% even in urban areas. The prevalence of diabetes in India is showing a sharp upswing as is evident from secular trends from different parts of the subcontinent, both in the urban and rural areas with a rough urban-rural divide of 2:1 or 3:1 being maintained through the last 2 - 3 decades with the exception of Kerala where rural prevalence rates have caught up with or even overtaken urban prevalence rates [14]. The probable explanation for this phenomenon is that in Kerala, there is indeed no clear urban/rural demarcation and the whole of Kerala can now be considered to be urbanized.

Studies on diabetes-Northern region

Table 1 is a compilation of studies on the prevalence of Type 2 diabetes in northern region of India from 1966 to 2007 in urban and rural areas (5, 15-27). It is evident from the table that Type 2 diabetes is more prevalent in the urban than in the rural populations. The earliest documented study on prevalence of diabetes in this region was done in urban area of Chandigarh in 1966 [15]. Prevalence studies in the rural areas were conducted in 1991, which reported that the prevalence of diabetes in a rural locality near Delhi was 1.5 % [18]. The prevalence has been reported to vary between 1.5 % in Delhi (1991) and 3.7% in Nagpur (2007) in rural areas. A prevalence of 4.6% was reported in 1994 from Pohir, a rural area in Punjab, which was relatively higher compared to earlier surveys done in different cities in that decade [19].

Regarding urban prevalence, an increasing trend is observed in the northern part of India since late 1960's, which has escalated from 2.9% in Chandigarh (1966) [5] to 20.1% in Jaipur (2007) [26]. Misra et al [21] reported a prevalence of 10.3% in a slum area in Delhi. Regarding IGT, the Kashmir valley study reported a high prevalence of 8.1 % and it was also observed that the prevalence was significantly higher in women [20].

Studies on diabetes-Southern region

The first study done in South India was at Vellore in 1964 [28]. This hospital based study done on 63,356 individuals showed a prevalence of 2.5%. The early signs of the looming diabetes epidemic were seen in the study conducted in Hyderabad in the year 1966, which reported a high prevalence of 4.1% [6]. However, the studies in rural areas were conducted since 1972 [29]. In 1984, house to house surveys were conducted in individuals aged 15 years and above in Tenali, a small town in Andhra Pradesh (urban) and rural population of Pondicherry (now Puducherry), which reported a prevalence of 4.7% [30] and 1.8% [31] respectively.

Table 2 presents studies on the prevalence of diabetes in southern region of the subcontinent [6,7,18,29,32-41]. The prevalence in south India has been reported to vary between 0.7% in Pondicherry to 19.5% in Kochi in urban areas, while the prevalence in rural areas range from 1.3% in Trivandrum to 13.2% in Godavari. It can be observed from the data provided in Table 2, that Chennai is perhaps the only city in south India where a series of population based studies have been done which has enabled the investigators to compare the prevalence rates. Studies have shown that the prevalence of type 2 diabetes had risen to 11.6% in the same urban area which had a prevalence of 8.2% five years earlier [34, 33]. In this region a study conducted in the peri-urban population has reported the prevalence rate to be midway between the rural and urban populations (5.9%) [42].

The Chennai Urban Rural Epidemiology Study (CURES) investigators had a unique opportunity to compare prevalence rates of diabetes in Chennai city with three earlier epidemiological studies carried out in the same city using similar methods [10, 34, 35]. The overall crude prevalence of diabetes using WHO criteria in CURES was 15.5 percent (age standardized: 14.3%) [39]. From 1989 to 1995, the prevalence of diabetes in Chennai increased by 39.8 percent (8.3 to 11.6%); between 1995 to 2000 by 16.3 percent (11.6 to 13.5%) and between 2000 to 2004, by 6.0 per cent (13.5 to 14.3%). Thus within a span of 14 years, the prevalence of diabetes increased significantly by 72.3 per cent **(Figure 3).** The CURES, however has reported a decreased prevalence of IGT compared to earlier studies done in Chennai (16.8% in 2000 to 10.2% in 2004), a decrease by 39.3% between 2000 and 2004 [10, 39]. This could suggest that the diabetes epidemic in urban India may be slowing down or it may also suggest that there could be a rapid progression from the normal state through IGT to diabetes, which could imply a rapid increase in the diabetes epidemic or a worsening diabetogenic environment. Further support of this hypothesis came from the ADEPS which showed a lower prevalence of 4.2% of IGT [41]. However, the ADEPS reported a high prevalence of IFG (11.2%). Thus prospective studies are required to assess the exact changes occurring with regard to the diabetes epidemic in India.

It has been shown that Indians have a younger age of onset of diabetes compared to other ethnic groups [43]. An increase in the prevalence of type 2 diabetes in the younger age group has been noted from the epidemiological studies. The CURES study demonstrated that there was a shift in the age at diagnosis of diabetes to a younger age compared with NUDS **(Figure 4)** [39]. Hence it is increasingly becoming apparent that type 2 diabetes has become prevalent even among younger age groups, which could have long lasting effects on the health of the nation and its economy. Thus it is clear that in the last two decades, there has been a marked increase in the prevalence of diabetes among urban south Indians. A similar

though slower trend is also shown among peri urban population and rural residents also [42].

Studies on diabetes- Eastern and Western regions

The earliest documented study on prevalence of diabetes in eastern region of India was a hospital based study done in Calcutta in 1938 [3]. There are very few epidemiological studies from this part of the region, which have looked at the prevalence of diabetes. The studies conducted have been done in metros alone or only in small towns or villages [10-12, 18, 44, 45]. Table 3 presents the epidemiological studies done in this part of India [18, 44, 45]. The prevalence of diabetes in urban areas has increased from 2.3% in 1975 to 11.7% in the year 200. A study conducted by in Manipur by Singh et al [46] in 2001 reported the prevalence of diabetes in peri-urban population to be 4.0%.

Majority of the studies in the western part of India have been conducted in Mumbai and Ahmedabad as shown in Table 3 [8,10,10,47-49]. Regarding urban prevalence, an increasing trend is observed, which has escalated from 1.5% (1963) [47] to 9.3% in Mumbai (2001) [10]. A similar trend is observed in the rural areas - an increase from 3.9% in 1991 [18] to 9.3% in 2006.

Reasons for escalation in diabetes prevalence in India

Despite the diversity within India, a number of common predisposing factors can be found with regard to patterns of diabetes and rising prevalence rates. The reasons for the escalation in diabetes in Indians are i) geographic regions and migration ii) stronger genetic factors iii) aging; due to the control of infections, people tend to live longer and thus are more susceptible to age related diseases, particularly diabetes iv) increased insulin resistance v) lower birth weight; could lead to diabetes during adulthood and vi) environmental factors particularly associated with urbanization (obesity, diet, physical inactivity). As observed, throughout India, the prevalence of diabetes is lower in rural areas, but the rate increases significantly from rural to peri-urban and higher in urban areas. The prevalence of diabetes in urban areas of India (12.1%) [10] is comparable to Indians in western countries as shown by the Daryaganj and the Southhall survey [50,51] where similar age standardised prevalence rates were found. This indicates ethnic (? genetic) susceptibility to diabetes in Indians which manifests with exposure to common environmental factors [52].

Studies have shown that the prevalence of diabetes increases with increasing family history of diabetes. In the NUDS, a positive family history of diabetes was found in 16.9% of diabetes subjects in NUDS [10]. A study done in south India reported the prevalence among offspring with one diabetic parent to be 36%, which increased to 54% when there was a positive family history of diabetes on the non-diabetic parental side also. When both parents had diabetes, the prevalence rate increased further (62%) [53]. Age and gender adjusted prevalence of diabetes was significantly higher in those with a family history (28.1 %) than in those without a family history (11.4%) and this difference was significant. In the Chennai Urban Population (CUPS) study, 55% of offspring of two diabetic patients had either diabetes or IGT compared to 15.6% in those with no family history of diabetes [38]. Thus it is clear that a large proportion of diabetic subjects in India have a history of diabetes in first or second degree relatives.

The important conclusion from various studies appears to be that such risk factors tend to develop early in the life cycle in developing countries like India and, consequently, diabetes occurs at least 10-15 years earlier in residents of this region than

in residents of developed countries [54,55]. Another imperative factor contributing to increased Type 2 diabetes in Asian Indians is the fact that they have a greater degree of insulin resistance compared to Caucasians [56]. Mohan et al [57] first demonstrated that Asian Indians have higher insulin levels to a glucose load than Europeans (hyperinsulinemia). This has subsequently been confirmed by several studies [58, 59]. They also have high central adiposity and high percentage body fat in comparison with many other populations. These are features of insulin resistance, which worsens with even small increments in weight and with lack of physical activity. Urban-rural differences observed in plasma insulin responses could be explained at least by partly differences in BMI, diet and physical activity, indicating the strong influence of environmental factors on insulin resistance patterns.

Studies by Yajnik et al [60, 61] demonstrated that low birth weight is a contributor to insulin resistance among Indians. His group also showed that Indian neonates have higher insulin levels and greater adiposity even at birth compared to Caucasians [62]. A long term follow up study done in 2004, supports this hypothesis and shows that lower birth weight coupled with obesity in childhood and adolescence leads to very high rates of diabetes [63].

Rapid urbanization and globalization in South Asian countries promote mechanization, which leads to sedentariness and major deviations in the dietary pattern which are influenced by the varied cultural and social customs. Traditional dietary patterns are disappearing as Indians are adapting themselves to living in the more industrialized, urban environments that are brought about by globalization. The major dietary changes that urbanization and affluence bring about are, substitution of unrefined wheat, rice or millets by highly polished wheat or rice and increased intakes of fat in higher income groups. These changes are associated with increasing obesity. The role of obesity in the pathogenesis of Type 2 diabetes is complex and is confounded by many heterogeneous factors. The results of a study conducted in North India [64] indicated that there was a strikingly high prevalence of abdominal obesity and generalized obesity as determined by body fat percentage in type 2 diabetic individuals. Another study by Singh et al [65] showed that overweight/obesity and central obesity were significantly associated with diabetes.

Burden due to increasing diabetes epidemic in India:

The explosion of diabetes in India increases the propensity for developing a broad spectrum of irreversible complications. Microvascular and macrovascular disease causes considerable mortality and morbidity both among diabetic patients [66]. In Type 2 diabetes the risk of some of these complications (e.g. coronary artery disease) may start even before onset of diabetes sets in [67]. In 1996, Rema et al [68] observed that the prevalence of diabetic retinopathy in a clinic based study to be 34.1%. Dandona et al [69] had reported a prevalence of 22.6% in an urban South Indian population in the year 1999. A study done in Palakkad (Kerala State) reported a higher prevalence of 26.8% in self reported diabetic subjects [70]. A recent publication from the Chennai Urban Rural Epidemiology Study (CURES) Eye Study showed an overall prevalence of 17.6% of DR in an urban population, which shows that approximately 1 in every 5 diabetic individual, may develop DR [71]. A few studies, mostly clinic based have looked at the prevalence of diabetic nephropathy in India *[12-7A].* But most of these are clinic based reports. Unnikrishnan et al in 2007 [75] showed that prevalence of overt nephropathy was

2.2% and that of microalbuminuria was 26.9% in the Chennai population. Very recently, a population based data from our CURES group reported that the prevalence of neuropathy in urban population was 26.1% [76]. A study done in the year 2006, showed that foot ulcers and rates of amputations were more common among diabetic subjects in the rural area compared to their urban counterparts [77].

The results from the CUPS study have provided population based data on the prevalence of macro vascular complications and mortality in relation to diabetes in India. Type 2 diabetic subjects have an increased predilection for developing coronary artery disease (CAD) and other atherosclerotic manifestations. The prevalence of coronary artery disease was 21.4% among diabetic subjects compared to 9.1% in subjects with normal glucose tolerance [78]. Atherosclerosis as assessed by carotid IMT was also found to be higher in subjects with type 2 diabetes compared to those with normal glucose tolerance [79]. The prevalence of peripheral vascular disease (PVD) was higher in type 2 diabetic subjects compared to (6.3% vs 2.7% $p<0.001$) [80].

The CUPS also provided some evidence on the effect of type 2 diabetes on mortality rates in a population [81]. The overall mortality rates were nearly three-fold higher in diabetic subjects compared to non-diabetic individuals (18.9 vs 5.3 per 1000 person-years). The hazards ratio (HR) for all cause mortality for diabetes was found to be 3.6 compared to non diabetic subjects. Several clinic based studies from India have looked at the mortality trends in diabetes [66, 82- 84]. CAD appears to be leading cause of death in majority of these studies [82,83]. However, Bhansali et al [84] and Zargar et al [66] reported that infections were the leading cause of mortality in diabetic subjects.

Conclusion

It is clear that in the last two decades, there has been a marked increase in the prevalence of diabetes among both urban as well as the rural Indians, with a suggestion that Southern India has seen the sharpest increase. Subsequent studies confirmed this high prevalence of diabetes in urban south India. Although in rural India the prevalence of diabetes is much lower than in the urban population, even here the prevalence rates are rapidly rising, though clearly more studies are needed. Variations in the prevalence rates of diabetes in different urban populations of India are expected because of the large variation in the prevalence of cardiovascular risk factors in different regions and states [85, 86]. It is evident that there is a shift in age of onset to younger age groups, which is alarming and this could have adverse effects on the nation's economy. Hence, the early identification of at-risk individuals and appropriate intervention to increase physical activity, bring about changes in dietary habits could to a great extent help to prevent/ delay, the onset of diabetes and thus reduce the burden due to its associated complications in India.

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Table 1: Epidemiological studies of type 2 diabetes in Northern region of India

NORTH INDIA		Urban			Rural		
Place	**Year of publication**	**n**	**Age**	**P(%)**	**n**	**Age**	**P(%)**
Chandigarh [5]	1966	3846	30+	2.9	-	-	-
Lucknow [15]	1973	2190	20+	1.1	-	-	-
Delhi [16]	1974	2291	20+	2.7	-	-	-
Delhi [17]	1986	6878	20+	3.1	-	-	-
Delhi [18]	1991	2572	20+	4.1	992	20+	1.5
Delhi [19]	1991	-	-	-	999	20+	0.4
Punjab [19]	1994	-	-	-	1100	30+	4.6
Srinagar [20]	2000	1538	40+	5.2	4045	40+	4.0
Delhi [21]	2001	532	18+	10.3	-	-	-
Delhi [10]	2001	2300	20+	11.6	-	-	-
Jaipur [22]	2003	1091	20+	12.3	-	-	-
Jaipur [23]	2004	458	20+	16.8	-	-	-
Rajasthan [24]	2004	-	-	-	882	20+	1.8
Delhi [25]	2005	2122	20-59	15.0	-	-	-
Jaipur [26]	2007	1127	20+	20.1	-	-	-
Nagpur [27]	2007	-	-	-	924	30+	3.7

p (%)-Prevalence percent

Table 2: Epidemiological studies of type 2 diabetes in Southern region of India

SOUTH INDIA		Urban			Rural		
Place	Year of publication	n	Age	P(%)	n	Age	p(%)
Hyderabad [6]	1966	21396	20+	4.1	-	-	-
Chennai [7]	1966	5030	20+	5.6	-	-	-
Pondicherry [32]	1968	2694	20+	0.7	-		
Hyderabad [29]	1972	-	-	-	2006	20+	2.4
Gangavati [33]	1990	-	-	-	765	30+	2.2
Trivandrum [18]	1991	-	-	-	1488	20+	1.3
Chennai [34]	1992	900	20+	8.2	1083	20+	2.4
Chennai [35]	1997	2183	20+	11.6	-	-	-
Chennai [36]	1999	1198	20+	7.6	-	-	-
Trivandrum [37]	2000	518	20+	12.4	-	-	-
Bangalore [10]	2001	1359	20+	12.4	-	-	-
Chennai [10]	2001	1668	20+	13.5	-	-	-
Hyderabad [10]	2001	1427	20+	16.6	-	-	-
Chennai [38]	2003	1262	20+	12	-	-	-
Chennai [39]	2006	2350	20+	15.5	-	-	-
Godavari [40]	2006	-	-	-	4535	30+	13.2
Kochi [41]	2006	3069	18-80	19.5	-		-

p (%)-Prevalence percent

Table 3: Epidemiological studies of type 2 diabetes in Eastern and Western regions of India

INDIA		Urban			Rural		
Place	Year of publication	n	Age	P(%)	n	Age	p(%)
EASTERN REGION							
Kolkata [44]	1975	4000	20+	2.3	-	-	-
Kolkata [18]	1991	-	-	- 8.2	2375	20+	0.8
Guwahati [45]	1998	1016	20+	11.7	-	-	-
Kolkata [10]	2001	2378	20+		-	-	-
WESTERN REGION							
Mumbai [47]	1963	18243	20+	1.5	-	-	-
Mumbai [8]	1966	3200	20+	2.1	-	-	-
Ahmedabad [18]	1991		-	-	1294	20+	3.9
Mumbai [48]	2001	520	20+	7.5	-	-	-
Mumbai [10]	2001	2084	20+	9.3	-	-	-
Sindhudurg [49]	2006	-	-	-	1022	20+	9.3

p (%)-Prevalence percent

Figure 1 **LEGENDS TO FIGURES:**

Figure 1: Prevalence of type 2 diabetes in urban and rural areas in different parts of India (period of study -1972-75) [ref 9]

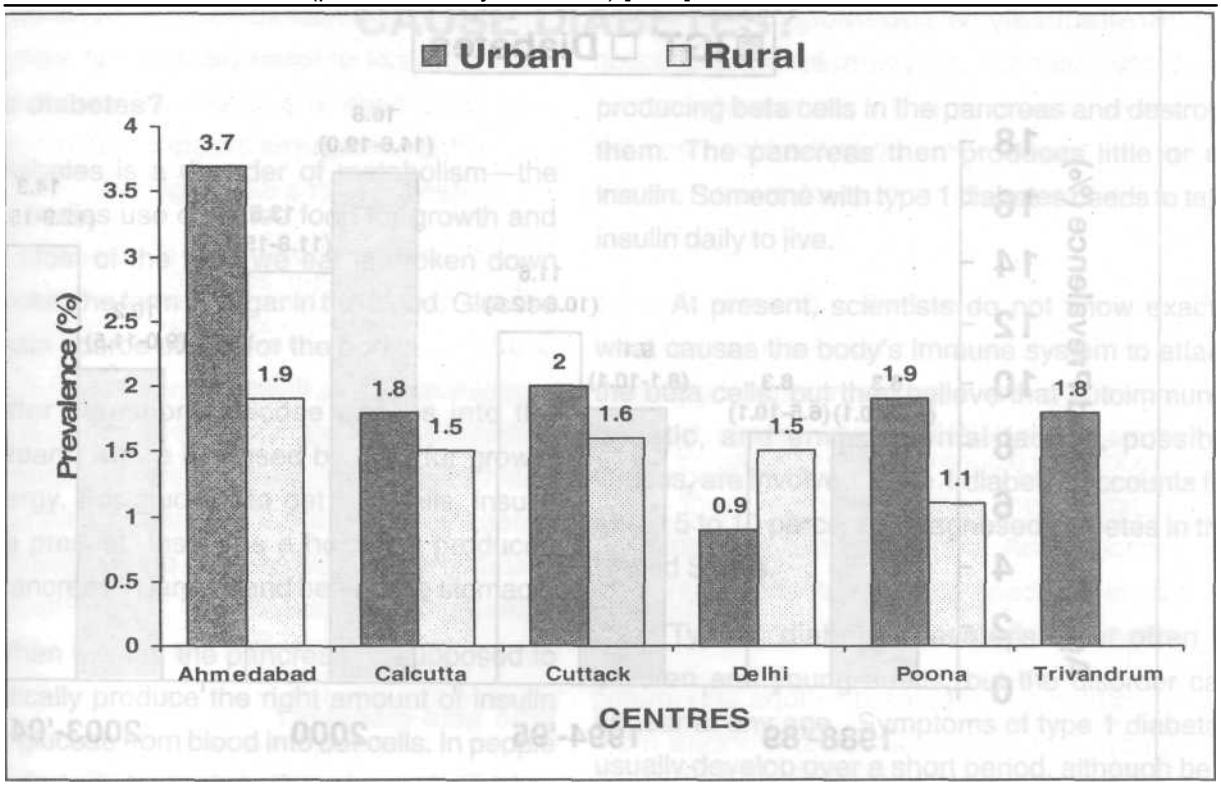

Figure 2 **Figure 2:** Region wise prevalence of self-reported diabetes in urban, periurban/slum and rural areas of India [ref 14]

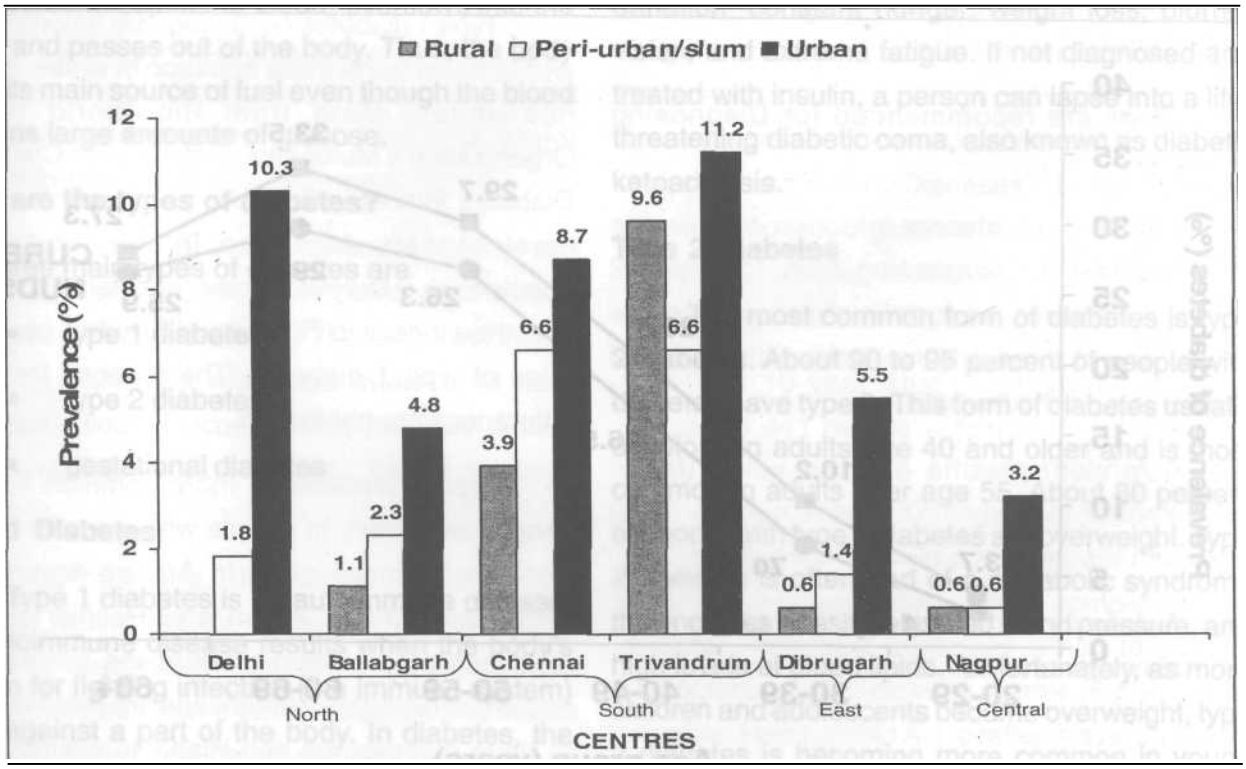

Figure 3

Figure 3: Secular trends in the prevalence of impaired glucose tolerance (IGT) and diabetes at Chennai [ref 39]

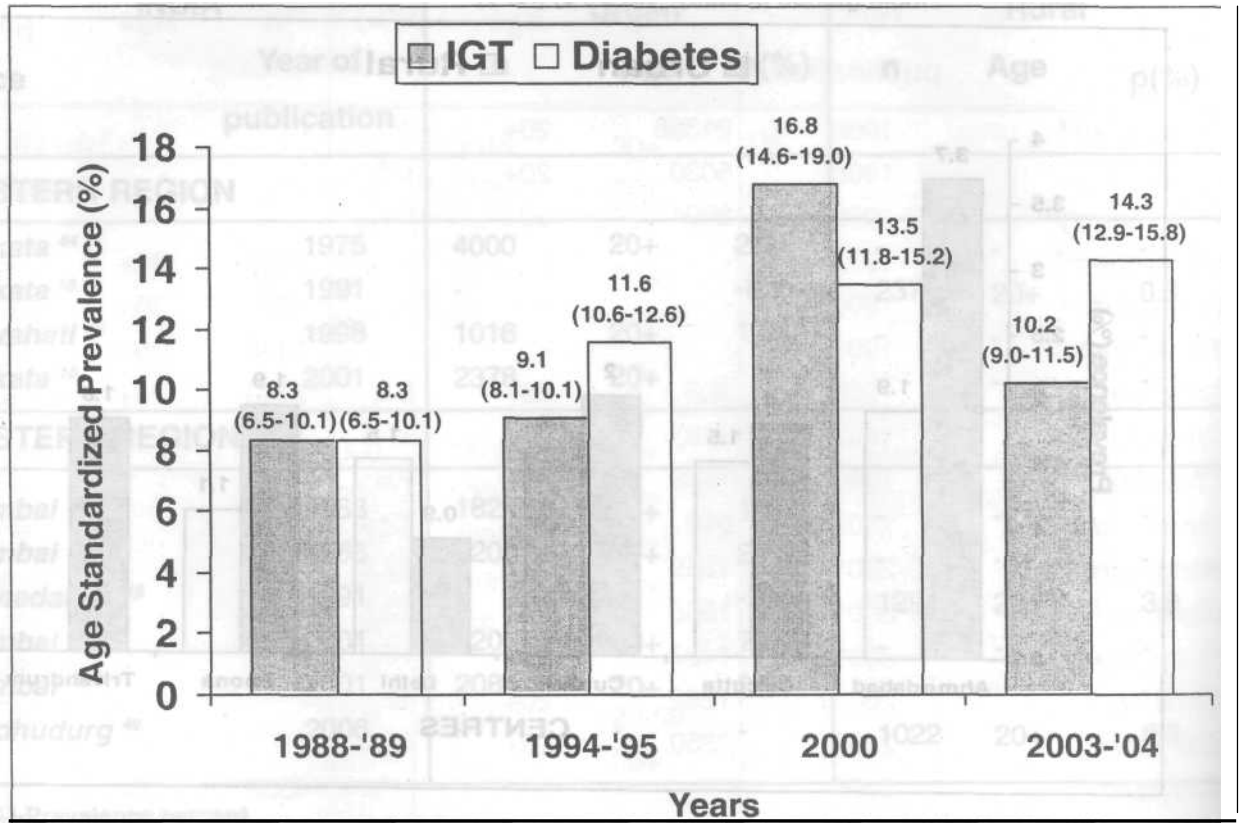

Figure 4: Age wise prevalence of diabetes Chennai urban rural epidemiology study (CURES) vs National Urban Diabetes Survey (NUDS) [ref 39]