Incidence of Diabetes and Pre-diabetes in a Selected Urban South Indian Population (CUPS - 19)

V Mohan*, M Deepa, RM Anjana, H Lanthorn, R Deepa

Abstract
Objectives: Several cross-sectional studies have reported on the prevalence of diabetes in India. However, there are virtually no longitudinal population-based studies on the incidence of diabetes from India. The aim of the study was to determine the incidence of diabetes and prediabetes in an urban south Indian population.

Methods: The Chennai Urban Population Study [CUPS], an ongoing epidemiological study in two residential colonies in Chennai [the largest city in southern India, formerly called Madras] was launched in 1996; the baseline study was completed in 1997. Follow-up examination was performed after a mean period of 8 years. At follow-up, 501 [47.0%] subjects had moved out of this colonies and were lost to follow-up. Of the remaining 564 individuals, 513 [90.9%] provided blood samples for biochemical analysis. Regression analysis was done using incident diabetes as dependant variable to identify factors associated with development of diabetes or pre-diabetes.

Results: Among subjects with normal glucose tolerance (NGT) at baseline [n=476], 64 (13.4%) developed diabetes and 48 (10.1%) developed pre-diabetes (IGT or IFG). The incidence rate of diabetes was 20.2 per 1000 person years and that of pre-diabetes was 13.1 per 1000 person years among subjects with NGT. Of the 37 individuals who were pre-diabetic at baseline, 15 (40.5%) developed diabetes [incidence rate: 64.8 per 1000 person years], 16 (43.2%) remained as pre-diabetic and 6 (16.2%) reverted to normal during the follow-up period. Regression analysis revealed obesity [Odds Ratio (OR): 2.1, p=0.001], abdominal obesity [OR: 2.23, p<0.001] and hypertension [OR: 2.57, p<0.001] to be significantly associated with incident diabetes. The Indian Diabetes Risk Score (IDRS) showed the strongest association with incident diabetes [OR: 5.14, p<0.001].

Conclusion: The study shows that the incidence of diabetes is very high among urban south Indians. While obesity, abdominal obesity and hypertension were associated with incident diabetes, IDRS was the strongest predictor of incident of diabetes in this population. ©

The Diabetes Atlas published by the International Diabetes Federation shows that India currently leads the world in number of people with diabetes and is currently home to over 40 million diabetic subjects. These numbers are predicted to increase to 69 million by 2025. Furthermore, India occupies the second position with respect to the number of subjects with impaired glucose tolerance (IGT). The above data has been compiled from several cross sectional studies done in various parts of India. However, to date, there is no longitudinal study on the incidence of diabetes or IGT in India. This paper reports on a eight year follow up study and presents the first incidence data on diabetes and prediabetes from India.

METHODS

Baseline study
The Chennai Urban Population Study [CUPS] is an ongoing epidemiological study conducted in two residential colonies representing the middle and lower income groups in Chennai [the largest city in southern India, formerly called Madras]. CUPS was started in 1996 and the baseline study was completed in 1997. The methodological details and several reports from CUPS have already been published. Briefly, all individuals ≥ 20 years of age living in these two colonies were invited to participate in a screening programme for diabetes and the overall response rate was 90.2%. The baseline study included anthropometry [weight, height, waist and hip] and blood pressure measurements using standard methods. The fasting sample was obtained, after ensuring 8 hours of overnight fast, for
estimation of glucose and lipids following this, an oral glucose load [75 gm] was administered to all individuals [excluding known diabetic subjects]. All biochemical assays (plasma glucose and lipids) were done using Hitachi 912 Autoanalyser (Roche Diagnostics GmbH, Mannheim, Germany) utilizing kits supplied by Roche Diagnostics GmbH (Mannheim, Germany). Individuals were categorized based on a validated physical activity [PA] questionnaire as having light, moderate or heavy activity. Of the 1262 subjects recruited at baseline, 152 had diabetes and were excluded from follow-up. Of the remaining 1110 individuals with either normal glucose tolerance (NGT) or IGT at baseline, 49 [4.4%] died during the follow-up period, leaving a total of 1061 study subjects.

Follow-up data on incidence of diabetes

Follow-up examination was performed after a mean period of 8 years. At follow-up, 497 (46.8%) subjects had moved out of the colonies and were deemed lost to follow-up after repeated attempts to trace them proved futile. Of the remaining 564 individuals still living in the two colonies, 513 (90.9%) participated in this study. The flow chart of the baseline and follow-up status of the study cohort is shown in Fig. 1.

Of the 513 respondents, 37 had been diagnosed to have diabetes by a physician and were on drug treatment for the same. These 37 subjects provided fasting and post prandial plasma glucose samples. Of the remaining 476 subjects, 340 (71.5%) individuals agreed to undergo an oral glucose tolerance test (OGTT), while the remaining 136 individuals agreed for a fasting plasma glucose estimation.

Definitions

Diabetes: Diabetes was diagnosed if the fasting plasma glucose was ≥126 mg/dl (≥7 mmol/l) or 2 hour post glucose was ≥200 mg/dl (≥11.1 mmol/l). Pre-diabetes: Pre-diabetes was diagnosed if the fasting plasma glucose was ≥110 (≥6.1 mmol/l) and <126 mg/dl (<7 mmol/l) – impaired fasting glycemia (IFG) or 2 hour post glucose was ≥140 mg/dl (≥7.8 mmol/l) and <200 mg/dl (<11.1 mmol/l) – impaired glucose tolerance (IGT).

Indian Diabetes Risk Score: The Indian Diabetes Risk Score (IDRS) described by Mohan et al was calculated in all individuals as described previously. IDRS is calculated using four simple parameters, age, family history of diabetes, physical activity and waist circumference. Statistical Analysis:

All the data were computed and statistical analyses was done using the SPSS PC Windows version 10.0 (Chicago, IL). Students “t” test was used to compare means between groups. Chi square test was used to compare proportions. Triglyceride values were log transformed to obtain normal distribution. Regression analysis was used to assess factors associated with development of diabetes. Cox regression analysis was used to determine the effect of various risk factors on diabetes. Survival curves were plotted by life table analysis and those of subjects with and without IGT at baseline and subjects with different IDRS scores were compared using Wilcoxon [Gehan] test. p<0.05 was considered to be statistically significant.

Results

There was no significant difference in the baseline characteristics of the current residents of the colonies (n=564) and those lost to follow-up (n=497). Current residents vs. lost to follow-up: age: 41±13 vs. 40±15 years, p=0.451; body mass index (BMI): 22.4±4.2 vs. 22.2±4.6 kg/m², p=0.343; waist circumference: 76.0±12.6 vs. 75.5±13.4 cm, p=0.517 and fasting plasma glucose: 76±17 vs. 75±19 mg/dl, p=0.265. The proportion of subjects with impaired glucose tolerance (IGT) was also not significantly different; current residents vs. lost to follow-up: 39 (6.9%) vs. 34 (6.8%), p=0.962.

Among the current residents (n = 564), 51 individuals refused to participate in the study. The comparison of the responders (n = 513) with the non-responders (n = 51) showed no significant difference in their baseline characteristics except for age. Responders vs. non-responders: age: 40±13 vs. 46±17 years, p=0.002; BMI: 22.5±4.2 kg/m² vs. 21.6±3.8 kg/m², p=0.136; waist circumference: 76.3±12.6 cm vs. 73.1±12.7 cm, p=0.080, fasting plasma glucose: 76±17 mg/dl vs. 73±16 mg/dl, p=0.132, systolic blood pressure (120±16 mmHg vs. 123±16 mmHg, p=0.147) and diastolic blood pressure (78±9 mmHg vs. 80±11 mmHg, p=0.181). The proportion of subjects with IGT was also not significantly different between the responders and non-responders: 7.2% vs 3.9%, p=0.377.

During the mean follow up period of 8±1.3 years, overall 79/513 (15.4%) developed diabetes, yielding an incidence rate of diabetes of 20.2 per 1,000 person years [79/3912X1000].

Among NGT subjects at baseline [n=476], 64 (13.4%) developed diabetes and 48 (10.1%) developed pre-diabetes. Thus the incidence rate of diabetes among NGT subjects was 17.5 per 1000 person years [64/3665 X1000] for diabetes and 13.1 per 1000 person years for pre-diabetes [48/3665X1000].

Of the 37 pre-diabetic individuals at baseline, 15 (40.5%) developed diabetes (incidence rate: 64.8 per 1000 person years [16/247X1000]), 16 (43.2%) remained pre-diabetic and 6 (16.2%) reverted to normal during the follow-up period. The proportion of pre-diabetic subjects at baseline who developed diabetes [40.5%] was significantly higher compared to the NGT subjects [13.4%] at baseline [p<0.0001] [Fig. 1].

Table 1 compares the characteristics of the NGT subjects at baseline who converted to diabetes and pre-
diabetes at follow-up compared to those who maintained as NGT. Compared with the “non-converters”, the “converters” were older at follow-up \( [p<0.05] \) and had increased BMI \( [p<0.05] \), waist circumference \( [p<0.05] \), systolic blood pressure \( [p<0.05] \), diastolic blood pressure \( [p<0.05] \) and fasting plasma glucose \( [p<0.05] \). Mean IDRS value was higher among converters compared to non-converters. Moreover, the proportion of subjects with IDRS \( \geq 60 \) was higher among converters compared to non-converters.

Incidence of diabetes at follow-up (per 1000 person years) increased with age at baseline: age: 20-29 years: 10.3; 30-39 years: 20.7; age: 40-49 years: 25.2 and \( \geq 50 \) years: 23.4.

Table 2 shows the clinical and biochemical factors associated with conversion to diabetes from either NGT or pre-diabetes status. The proportion of subjects developing diabetes was significantly higher among subjects with one parent diabetic \( [20.7\%] \) as compared with neither parent diabetic, and still higher in subjects with both parents diabetic \( [35.7\%] \). More obese subjects \( [24.5\%] \) converted to diabetes than non-obese subjects \( [12\%] \). More subjects with abdominal obesity \( [28.1\%] \) converted than those without abdominal obesity \( [10.7\%] \) at baseline. Subjects with hypertension at baseline had significantly higher prevalence of diabetes at follow-up. However, there was no significant difference in the proportion of subjects who developed diabetes with reference to physical activity at baseline.

Table 2 also shows the relative risk (RR) for diabetes based on various parameters. Subjects with obesity at baseline had a relative risk of 2.1 for diabetes \( [95\% \text{ CI}: 1.35 – 3.29] \). Introducing age and gender into the model did not significantly alter the results. Similar results were observed with abdominal obesity. However, family history of diabetes, hypertriglyceridemia and hypercholesterolemia failed to show an association with diabetes in this model. Subjects with IDRS \( \geq 60 \) at baseline had the highest proportion of conversion to diabetes (27.8\%) compared to those with score of 30-50 (16.9\%) and <30 (5.6\%) \( p<0.001 \). Moreover, 38.4\% of ‘converters’ to either diabetes or pre-diabetes had IDRS \( \geq 60 \) at baseline. We computed the relative risk for IDRS and observed that IDRS had a significant association with diabetes even after adjusting for age and gender [Table 2], [IDRS \( \geq 60 \): RR 3.1, \( p=0.035 \), IDRS 30 – 50: RR 2.7, \( p=0.032 \)].

The life table analysis using Wilcoxon (Gehan) statistic test revealed a statistically significant difference in development of diabetes between subjects with IDRS \( \geq 60 \) compared to those with IDRS 30-50 and IDRS <30 [\( p=0.0003 \)] [Fig. 2].

**DISCUSSION**

This is the first study to our knowledge, to present the incidence of diabetes and prediabetes in Indians. This is significant, given that India is the epicentre of

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**Table 1 : Baseline characteristics of the NGT subjects based on their glycemic status at follow-up**

<table>
<thead>
<tr>
<th></th>
<th>Remained as NGT (NGT to NGT) [n = 364]</th>
<th>Converters to Pre-diabetes (NGT to IFG or IGT) [n = 48]</th>
<th>Converters to Diabetes (NGT to DM) [n = 64]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>38 ± 12</td>
<td>45 ± 13 *</td>
<td>43 ± 14 *</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.8 ± 4.1</td>
<td>23.5 ± 3.4 *</td>
<td>24.4 ± 4.4 *</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>74.2 ± 11.9</td>
<td>78.7 ± 13.7 *</td>
<td>82.2 ± 11.8 *</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.83 ± 0.08</td>
<td>0.85 ± 0.08</td>
<td>0.89 ± 0.11 *</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>118 ± 16</td>
<td>122 ± 15</td>
<td>127 ± 19 *</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>77 ± 9</td>
<td>79 ± 8</td>
<td>81 ± 11 *</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>75 ± 13</td>
<td>81 ± 14 *</td>
<td>81 ± 18 *</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>167 ± 41</td>
<td>179 ± 38</td>
<td>169 ± 56</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
<td>110 ± 69</td>
<td>121 ± 62</td>
<td>115 ± 60</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>39 ± 11</td>
<td>41 ± 11</td>
<td>36 ± 16</td>
</tr>
<tr>
<td>Family history of diabetes n(%)</td>
<td>59 (16.2)</td>
<td>13 (27.1)</td>
<td>18 (28.1) *</td>
</tr>
<tr>
<td>Mean Indian diabetes risk score (IDRS)</td>
<td>35.7 ± 15.7</td>
<td>44.2 ± 13.7 *</td>
<td>45.1 ± 15.0 *</td>
</tr>
<tr>
<td>Subjects with IDRS score ≥ 60 n(%)</td>
<td>38 (10.4)</td>
<td>7 (14.6)</td>
<td>15 (23.8) *</td>
</tr>
</tbody>
</table>

* \( p<0.05 \) compared to subjects who remained as NGT and \# \( p<0.05 \) compared to converters to IGT.
the world’s diabetes epidemic. The main findings of this study are: (1) incidence of diabetes in this urban south Indian population was 20.2 per 1,000 person years, (2) incidence of pre-diabetes was 13.1 per 1,000 person years, (3) incidence of diabetes among subjects with IGT at baseline was higher compared to those with NGT and (4) the Indian Diabetes Risk Score (IDRS) developed by us seems to be the best predictive tool of incident diabetes in Asian Indians.

Other studies have examined the progression from IGT to diabetes. A study from Baltimore reported that 17% of subjects with IGT progressed to diabetes during 10 years of follow up.12 Similar results were observed in Taiwan.13 In the present study, over 40% of subjects with IGT at baseline developed diabetes during 8 years of follow-up, translating to an incidence rate of 64.8 per 1000 person-years which is very high.

In terms of overall incidence, Dowse et al found that among Pacific and Indian Ocean populations, Pima Indians (Native Americans) had the highest diabetes incidence rate (15 per 1000 cases per 1000 person-years) along with rural Wanigelas, (Papua New Guinea), Nauruans (Micronesia), urban Samoans and finally Asian Indians in Mauritius.14 In the present study, the incidence rate among NGT at baseline subjects was 17.5 per 1000 person-years. Both this and Dowse et al’s findings from other Pacific and Indian Ocean populations are much higher than what is reported from other ethnic groups,15-17 suggesting once again the existence of the so called ‘Asian Indian Phenotype’18,19 with an increased susceptibility to diabetes.

In an earlier clinic based study conducted in South India, we showed that one-third of IGT subjects, while one-third remained as IGT and one-third reverted back to normal.20 In another clinic based study,21 54 individuals with IGT were followed for a median of 7.0 years, 14 (25.9%) developed diabetes and 16.2% reverted to normal. In the present study, 40.5% developed
diabetes and 33.4% reverted to normal. This difference in conversion rates could be due to the marked changes in environmental factors over the past 10 years. Moreover only the present study is population based.

Determining the conversion rates to diabetes in a population is important as it reveals the future burden of diabetes. According to the International Diabetes Federation report, presently India has 35.9 million IGT subjects. We found that the incidence of diabetes in subjects with IGT is 64.8 / 1000 person years. Thus, in a period of one year, 2.2 million subjects with IGT will likely convert to diabetes. In addition, the present study shows that another 1.7 million people, currently with NGT status, will convert in one year. These numbers suggest a dramatic increase and an alarming health and economic threat due to diabetes in India.

Given that diabetes is an expensive and debilitating disease, it is worthwhile to look for risk factors associated with incident diabetes. In this study, age, waist (that is, abdominal obesity) and BMI (that is, generalized obesity) are seen to be causative factors. Earlier studies also strongly implicated both generalized and abdominal obesity as risk factors for diabetes. Intervention studies have proved that a 5-7% reduction in the weight of high-risk subjects could produce a decline in the incidence of diabetes. To put this information to use, we need to identify high-risk individuals to prevent or delay the onset of diabetes. Screening a whole population to identify undiagnosed diabetic subjects may be expensive and laborious. Hence, recent studies have focused on diabetes risk scores for opportunistic screening. The Indian Diabetes Risk Score (IDRS) was derived by us as a simple tool for detecting undiagnosed diabetes with sensitivity of 72.5% and a specificity of 60.1%. In this study, IDRS showed the strongest association with diabetes. The risk contributed by IDRS ≥ 60 at baseline was 3 times higher than that from low-risk subjects (IDRS <30). Moderate risk subjects (IDRS 30 - 50) had 2 times higher risk for diabetes compared to those with low risk (IDRS <30). This indicates that IDRS has excellent predictive value for diabetes and is much stronger than examining risk factors individually. IDRS is therefore, more suitable for opportunistic screening. In addition, it can help to identify metabolic syndrome and coronary artery disease.

The limitations of this study are (1) the small numbers of subjects studied and (2) follow-up rate of 53.2% due to constant migration of the population. However, those lost to follow-up were not significantly different from those retained in the study. Hence, we presume that this would not have significantly affected the results of the study. The strength of this study is that it is the first longitudinal population based study from India to report on incidence rates of diabetes and prediabetes.

In conclusion, this study reports that incidence rates of diabetes and prediabetes in India are higher compared to other ethnic groups and western populations and that the Indian Diabetes Risk Score (IDRS) is perhaps the best predictor of incident diabetes among Asian Indians.

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REFERENCES


14. Dowse GK. Incidence of NIDDM and the natural history of IGT


Announcement

The following members were awarded the Fellowship of the ICP at Kochi, APICON 2008

1. Dr. Sunil Agarwal Delhi 16. Dr. A Murugananthan Tirupur
2. Dr. Madhu Sudan Barthwal Ranchi 17. Dr Prabhu Dyal Pahwa Gurgaon
3. Dr. Richa Dewan New Delhi 18. Dr. Abhijit Pal Kolkata
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