Incidence of Diabetes and Prediabetes and Predictors of Progression Among Asian Indians: 10-Year Follow-up of the Chennai Urban Rural Epidemiology Study (CURES)

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OBJECTIVE

There are few data on the incidence rates of diabetes and prediabetes (dysglycemia) in Asian Indians. This article presents the incidence of diabetes and prediabetes and the predictors of progression in a population-based Asian Indian cohort.

RESEARCH DESIGN AND METHODS

Data on progression to diabetes and prediabetes from 1,376 individuals, a subset of 2,207 of the Chennai Urban Rural Epidemiology Study (CURES) cohort (phase 3) with normal glucose tolerance (NGT) or prediabetes at baseline, who were followed for a median of 9.1 years (11,629 person-years), are presented. During follow-up, 534 died and 1,077 with NGT and 299 with prediabetes at baseline were reinvestigated in a 10-year follow-up study. Diabetes and prediabetes were diagnosed based on the American Diabetes Association criteria. Incidence rates were calculated and predictors of progression to prediabetes and/or diabetes were estimated using the Cox proportional hazards model.

RESULTS

The incidence rates of diabetes, prediabetes, and "any dysglycemia" were 22.2, 29.5, and 51.7 per 1,000 person-years, respectively. Among those with NGT, 19.4% converted to diabetes and 25.7% to prediabetes, giving an overall conversion rate to dysglycemia of 45.1%. Among those with prediabetes, 58.9% converted to diabetes. Predictors of progression to dysglycemia were advancing age, family history of diabetes, 2-h plasma glucose, glycated hemoglobin (HbA_{1c}), low HDL cholesterol, and physical inactivity.

CONCLUSIONS

Asian Indians have one of the highest incidence rates of diabetes, with rapid conversion from normoglycemia to dysglycemia. Public health interventions should target modifiable risk factors to slow down the diabetes epidemic in this population.

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A slide set summarizing this article is available online.

The South Asian region is characterized by high prevalence rates of type 2 diabetes, in spite of having a young population with relatively low levels of obesity (1). To explain this phenomenon, the existence of a "South Asian" or an "Asian Indian" phenotype has been postulated. This phenotype is characterized by higher waist circumference, higher levels of total and visceral fat, hyperinsulinemia, insulin resistance, and a greater predisposition to diabetes as compared with white Caucasians of comparable BMI (2). Although a few studies on migrant south Asians (3,4) and one small study of a highly selected population of native Asian Indians (5) have attempted to assess the incidence rates of diabetes in this important ethnic group, there has been, to date, no large population-based study from this region assessing the incidence rates of diabetes and the rates of conversion through different stages of dysglycemia. This is particularly of relevance as recent studies report higher rates of diabetes among native Asian Indians compared with migrant Indians.

In this article, we attempt to *1*) estimate the incidence rates of diabetes and prediabetes, *2*) study the conversion rates from normal glucose tolerance (NGT) to various categories of dysglycemia, and *3*) assess the predictors of progression, in the follow-up cohort of a large epidemiological survey, conducted on a representative population in Chennai, the largest city in South India.

RESEARCH DESIGN AND METHODS

Study Population

The present article reports on the results of the follow-up of the Chennai Urban Rural Epidemiology Study (CURES) cohort. The methodology of CURES has been published elsewhere (6). Figure 1 is a flow diagram describing the selection of study participants. In brief, CURES was performed on a representative sample of 26,001 adults ≥20 years of age from Chennai. The baseline survey was carried out between 2001 and 2003. In the baseline survey, of the 26,001 individuals screened, all the individuals with diabetes (phase 2, *n* = 1,382) and 1 in every 10 individuals (phase 3, *n* = 2,207) underwent further detailed investigations, and these constituted the cohort for this follow-up study (*n* = 3,589). Of these, 645 individuals were lost to follow-up (18%). This includes 636 individuals who had migrated and were not traceable and 9 who refused to participate even after repeated attempts. At follow-up, 534 individuals died (14.9%), of whom, verbal autopsy was available in 381 individuals. Of these, 299 had diabetes at baseline and were excluded, and 82 individuals had either NGT (*n* = 55) or prediabetes (*n* = 27) at baseline. Of these, those individuals whose glycemic status was unknown at follow-up (*n* = 53) were further excluded and only those individuals on whom glucose tolerance status at follow-up was known (*n* = 29, 15 with NGT and 14 with prediabetes at baseline) were included in the analysis. Among those individuals who were alive, the follow-up was completed in 2,410 individuals (1,062 individuals with NGT, 285 with prediabetes, and 1,063 with diabetes at baseline). Of these, all those who had diabetes at baseline (*n* = 1,063) were excluded, and the final results for 1,376 individuals (1,077 with NGT and 299 with prediabetes) are presented. Thus the completion rate for the current analysis is 62.3% (1,376 out of 2,207).

Demographic, Lifestyle, and Anthropometric Assessment

The following investigations were performed both at baseline and follow-up visit. Details pertaining to demography, socioeconomic status, medical and family history, physical activity, and tobacco and alcohol use were elicited using a structured, pretested, and validated interviewer-administered questionnaire. Physical activity was dichotomously coded as active (moderate or vigorous intensity physical activity achieving at least 600 metabolic equivalent minutes per week) or inactive (those not meeting the above criteria). Family history of diabetes was considered as positive if either or both the parents had diabetes. Smokers were defined as those who were currently smoking, and alcohol use was defined as current alcohol consumption. Anthropometric details (such as height, weight, waist circumference, and hip circumference) and blood pressure (BP) were measured using standardized techniques (6). Waist-to-hip ratio was defined as the ratio between waist and hip circumference, and abdominal obesity was defined as waist circumference ≥80 cm for males and ≥90 cm for females.

Biochemical Assessment

A venous blood sample was drawn in the fasting state and 2 h after oral administration of 75 g of glucose at the follow-up visit in all individuals who did not give history of development of diabetes in the interim. Biochemical analyses included fasting and 2-h glucose and insulin levels, serum lipids, and glycated hemoglobin (HbA_{1c}). Biochemical analyses were performed in a laboratory certified by the National Accreditation Board for Testing and Calibration Laboratories and the College of American Pathologists on a Hitachi 912 Autoanalyzer (Hitachi, Mannheim, Germany) using kits supplied by Roche Diagnostics (Basel, Switzerland) for estimation of plasma glucose (GOD-POD method), serum cholesterol (CHODPAP method), serum triglycerides (GPO-PAP method), and HDL cholesterol (direct method). HbA_{1c} was estimated by high-pressure liquid chromatography using the Variant machine (Bio-Rad, Hercules, CA). Based on the National Cholesterol Education Program–Adult Treatment Panel III Recommendations (7), high triglycerides were defined as serum triglyceride levels of 150 mg/dL (1.7 mmol/L) or above, and low HDL cholesterol was defined as HDL cholesterol <40 mg/dL (<1.03 mmol/L) for males and <50 mg/dL (<1.3 mmol/L) for females. Serum insulin concentration was estimated using the electrochemiluminescence method (cobas e 411; Roche Diagnostics). Insulin resistance was measured using the HOMA of insulin resistance method, using the formula [(fasting glucose in mg/dL × fasting insulin in mU/mL)/405] (8), and individuals with values >2.58 were considered to have insulin resistance (9). The intra- and interobserver coefficients of variation for the biochemical assays ranged from 3.1 to 7.6%.

Outcome Assessment

Diabetes was diagnosed at follow-up visit if the venous plasma glucose 2 h after oral glucose load (2-h plasma glucose [2-h PG]) was ≥200 mg/dL (11.1 mmol/L) and/or the fasting plasma glucose (FPG) levels were ≥126 mg/dL (7.0 mmol/L) (10). History of diabetes during the follow-up period was obtained through self-report. This was then checked against medical records for

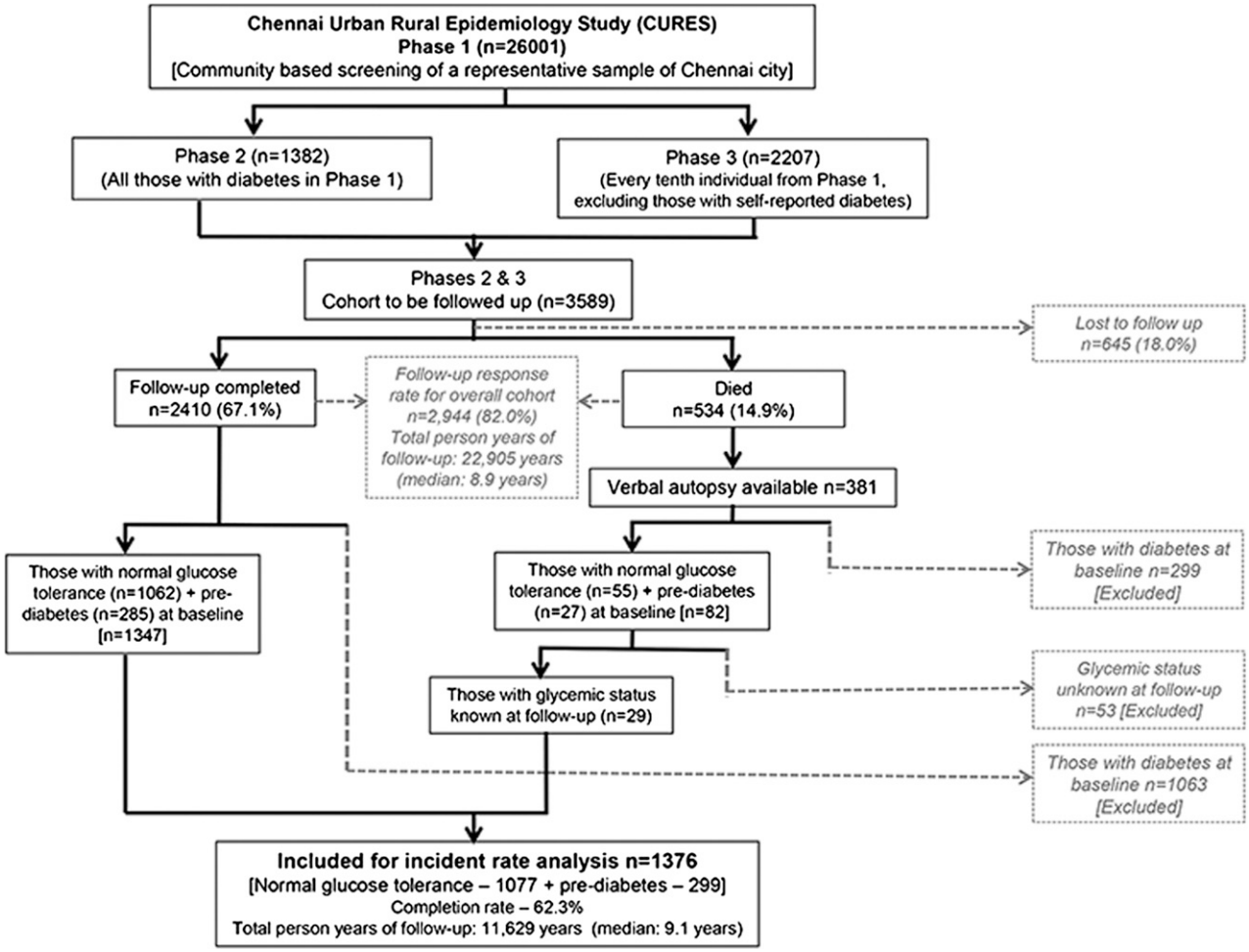

Figure 1—Flow diagram describing the selection of study participants. Lighter colored boxes represent subgroups that are essential for understanding the study methodology but are not directly relevant to the present analysis.

validity, which also helped to define the date and year of diagnosis.

Isolated impaired glucose tolerance (i-IGT) was diagnosed if 2-h PG was between 140 and 199 mg/dL (7.8–11.0 mmol/L), with FPG <100 mg/dL (5.6 mmol/L) (10). Isolated impaired fasting glucose (i-IFG) was diagnosed if FPG values were between 100 and 125 mg/dL (5.6–6.9 mmol/L), with 2-h PG <140 mg/dL (7.8 mmol/L) (10). Prediabetes was defined as FPG 100–125 mg/dL (5.6–6.9 mmol/L) or 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L), i.e., those with i-IGT or i-IFG or both. Dysglycemia was diagnosed if the individuals had diabetes or any one of the prediabetic states. NGT individuals were those with FPG <100 mg/dL (5.6 mmol/L) and 2-h PG <140 mg/dL (7.8 mmol/L) (10).

Death Ascertainment

Information on death was obtained from study participant family members. The cause of death was ascertained through medical records, death certificates, or discharge summaries from hospitals and a verbal autopsy was obtained. These documents were adjudicated by trained physicians.

Statistical Analyses

Statistical analyses were performed using SAS Statistical Package (version 9.0; SAS Institute, Inc., Cary, NC), Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL), and STATA package. Estimates are expressed as mean ± SD or median (interquartile range [IQR]) or proportions. One-way ANOVA was used to compare continuous variables between the three progression groups followed by Tukey post hoc and χ^2 tests, for categorical variables. Person-years for diabetes or prediabetes were calculated from the baseline examination until the event developed or death occurred or until the last examination, whichever came first. Incidence of diabetes with 95% CI was calculated per 1,000 person-years with the number of persons who developed diabetes during follow-up as numerator and the total person-time as denominator. Cox proportional hazards model was used to find the association between the various factors and progression to diabetes, prediabetes, and dysglycemia. The variables that had a P value <0.2 in univariate analysis or were clinically relevant were selected to enter into the Cox proportional hazards model. The risk factors included in the final model were age, sex, family history of diabetes, waist circumference, 2-h PG, HbA_{1c}, insulin resistance, serum triglycerides, low HDL cholesterol, physical inactivity, smoking, and alcohol. At baseline, we had missing data for a few variables, which could potentially influence the results. Hence, sensitivity analysis was performed to explore the potential influence of these variables on incident diabetes. Incident cases of diabetes

observed among missing and nonmissing values did not differ significantly, suggesting that missing data did not significantly alter our results. *P* value <0.05 (two-tailed) was considered significant.

RESULTS

The follow-up survey was performed in 2012–2013 after a median of 9.1 years (IQR 2.6) (11,629 person-years of follow-up). We found that 385 individuals progressed to diabetes, of whom, 116 were detected by the systematic oral glucose tolerance test performed at the 10-year follow-up examination and 269 developed diabetes (diagnosed by a physician, on antidiabetic drugs, or had values of diabetes diagnosis) before the final follow-up examination. The mean age at diagnosis of diabetes among the incident diabetes case subjects was 50.9 ± 12.8 years and the mean HbA_{1c} was 7.6 ± 1.8% (60 mmol/mol). Table 1 shows the incidence rates of diabetes and various categories of dysglycemia in the study population. Out of 1,077 individuals with NGT at baseline, 209 developed diabetes, yielding an incidence rate of diabetes of 22.2 per 1,000 person-years (95% CI 19.4–25.4). Among the 299 individuals with prediabetes at baseline, 176 developed diabetes (incidence rate of 78.9 per 1,000 person-years [68.0–90.9]). Overall, the incidence of diabetes for the entire cohort was 33.1 per 1,000 person-years (29.9–36.5) and the incidence of prediabetes was 29.5 per 1,000 person-years (26.1–33.1). Finally, the incidence of "any dysglycemia" was 51.7 per 1,000 person-years (47.3–56.4).

Overall, during the follow-up period, 19.4% of those with NGT converted to diabetes and 25.7% converted to prediabetes, giving an overall conversion rate to dysglycemia of 45.1%. Among those with prediabetes, 58.9% converted to diabetes (52.8% among i-IGT, 47.8% among i-IFG, and 84.1% among those with combined IFG and IGT). There were no sex-wise differences in the progression to dysglycemia in the study cohort (Supplementary Table 2).

If the World Health Organization cut point of 110 mg/dL (6.1 mmol/L) (11) were used for defining IFG, the incidence rate of prediabetes among those with baseline NGT would decrease to 19.4 per 1,000 person-years (95% CI 16.7–22.3) and that of "any dysglycemia" to 43.3 per 1,000 person-years (39.4–47.5). However, the incidence of diabetes among those with NGT at baseline would increase to 23.9 per 1,000 person-years (21.0–27.1) and incidence of diabetes among those with prediabetes at baseline to 84.2 per 1,000 person-years (71.7–98.2).

Table 2 shows the clinical and biochemical characteristics of individuals with NGT and prediabetes at baseline based on their glycemic status at follow-up. Individuals who progressed from NGT to prediabetes or diabetes were significantly older and had higher BMI, waist circumference, systolic and diastolic BP, FPG, 2-h PG, HbA_{1c}, fasting insulin, 2-h insulin, insulin resistance, serum cholesterol, and triglycerides, compared with those who did not. Among individuals with prediabetes at baseline, compared with those who regressed to NGT or remained as prediabetes, those who progressed to diabetes had significantly higher FPG, 2-h PG, and HbA_{1c} and were more likely to have a positive family history of diabetes and less likely to consume alcohol.

Table 3 shows the Cox proportional hazards models presenting the hazard ratios for incident diabetes, prediabetes, and dysglycemia in the study cohort. Overall, the predictors of progression to dysglycemia included advancing age, positive family history of diabetes, 2-h PG, HbA_{1c}, low HDL cholesterol, and physical inactivity. Age, 2-h PG, low HDL cholesterol, and physical inactivity were found to independently predict incident prediabetes, whereas family history of diabetes and HbA_{1c} were found to predict incident diabetes.

The incidence rates of diabetes and prediabetes were also estimated by levels of 2-h PG and HbA_{1c} at baseline. The risk of diabetes was seen to increase at 2-h PG levels of 6.1–7.1 mmol/L (110–129 mg/dL) and HbA_{1c} levels of

Table 1—Incidence rates of diabetes* and various categories of dysglycemia in the study cohort

Glucose tolerance status at baseline	*n*	Person-years	Glucose tolerance status at 10-year follow-up	Outcomes (*n*)	Rate per 1,000 person-years	95% CI
NGT	1,077	9,398	i-IGT	55	5.9	4.4–7.6
		9,398	i-IFG	161	17.1	14.6–20.0
		9,398	IFG-IGT	61	6.5	5.0–8.3
		9,398	i-IFG, i-IGT, or IFG-IGT	277	29.5	26.1–33.1
		9,398	Diabetes	209	22.2	19.4–25.4
		9,398	i-IFG, i-IGT, IFG-IGT, or diabetes	486	51.7	47.3–56.4
i-IFG	67	525	IFG-IGT	6	11.4	4.2–24.7
		525	Diabetes	32	61.0	42.1–85.0
		525	IFG-IGT or diabetes	38	72.4	51.7–98.0
i-IGT	163	1,269	IFG-IGT	9	7.1	3.2–3.4
		1,269	Diabetes	86	67.8	54.6–83.0
		1,269	IFG-IGT or diabetes	95	74.9	61.0–90.7
IFG-IGT	69	434	Diabetes	58	133.6	103.1–169.3
i-IFG, i-IGT, or IFG-IGT	299	2,231	Diabetes	176	78.9	68.0–90.9
NGT, i-IFG, i-IGT, or IFG-IGT	1,376	11,629	Diabetes	385	33.1	29.9–36.5

n = 1,376 (1,347 cases who were alive at the end of follow-up + 29 cases who developed diabetes but were not alive at the end of follow-up). i-IFG, i-IGT, IFG-IGT, and diabetes are categories of dysglycemia. IFG-IGT, combined IFG and IGT. *Diabetes criteria: FPG ≥126 mg/dL (7.0 mmol/L) or 2-h PG ≥200 mg/dL (11.1 mmol/L).

Table 2—Baseline characteristics of individuals with NGT (*n* = 1,077) and prediabetes (*n* = 299) based on their glycemic status at follow-up

	NGT at baseline (*n* = 1,077)					Prediabetes (IFG/IGT) at baseline (*n* = 299)				
		Remained as NGT	Progressed to prediabetes	Progressed to diabetes			Regressed to NGT	Remained as prediabetes	Progressed to diabetes	
		(NGT as NGT)	(NGT to IFG/IGT)	(NGT to DM)			(IFG/IGT to NGT)	(IFG/IGT as IFG/IGT)	(IFG/IGT to DM)	
Variables	*n*	(*n* = 591)	(*n* = 277)	(*n* = 209)	*P* value	*n*	(*n* = 52)	(*n* = 71)	(*n* = 176)	*P* value
Male, *n* (%)	445	256 (57.5)	107 (24.0)	82 (18.4)	0.203	128	26 (20.3)	30 (23.4)	72 (56.3)	0.282
Female, *n* (%)	632	335 (53.0)	170 (26.9)	127 (20.1)	0.203	171	26 (15.2)	41 (24.0)	104 (60.8)	0.282
Age (years)	1,077	35.7 ± 11.1	39.2 ± 12.0*	43.1 ± 12.1*#	<0.001	299	44.7 ± 15.3	44.7 ± 13.6	47 ± 13.1	0.367
BMI (kg/m^2)	1,074	22.9 ± 4.4	24.5 ± 5.0*	24.7 ± 5.0*	<0.001	298	24.9 ± 5.1	24.9 ± 4.1	25.8 ± 4.3	0.225
Waist, male (cm)	423	82.4 ± 11.9	85.7 ± 11.8	88.1 ± 10.5*	<0.001	125	88.1 ± 11.0	88.8 ± 13.8	92.1 ± 10.1	0.206
Waist, female (cm)	623	80.8 ± 12.1	84.8 ± 11.7*	87.2 ± 11.7*	<0.001	165	85.2 ± 10.7	87.0 ± 10.0	89.8 ± 12.1†	0.133
Waist-to-hip ratio	1,031	0.87 ± 0.10	0.88 ± 0.08	0.90 ± 0.07	0.001	277	0.91 ± 0.14	0.90 ± 0.09	0.91 ± 0.08	0.707
Systolic BP (mmHg)	1,076	115 ± 16	116 ± 16	121 ± 18*#	<0.001	299	128 ± 21	128 ± 19	129 ± 21	0.947
Diastolic BP (mmHg)	1,076	72 ± 11	74 ± 11	76 ± 11*	<0.001	299	76 ± 12	78 ± 10	78 ± 11	0.358
FPG (mg/dL)	1,077	82 ± 7	85 ± 7*	86 ± 7*	<0.001	299	94 ± 10	94 ± 10	98 ± 14†	0.022
2-h PG (mg/dL)	1,077	98 ± 19	103 ± 20	107 ± 19*#	<0.001	299	138 ± 31	146 ± 24	157 ± 25†‡	<0.001
HbA_{1c} (%)	1,069	5.4 ± 0.4	5.5 ± 0.5*	5.8 ± 0.5*#	<0.001	295	5.7 ± 0.5	5.8 ± 0.6	6.2 ± 0.7†‡	<0.001
HbA_{1c} (mmol/mol)	1,069	36	37*	40*#	<0.001	295	39	40	44†‡	<0.001
Fasting insulin (μIU/mL)§	775	(*n* = 403) 6.6	(*n* = 199) 7.3*	(*n* = 173) 9.0*	<0.001	180	(*n* = 33) 11.0	(*n* = 56) 10.0	(*n* = 145) 11.0	0.615
2-h PG insulin (μIU/mL)§	772	(*n* = 402) 36.6	(*n* = 197) 40.4*	(*n* = 173) 49.4*	<0.001	178	(*n* = 33) 66.7	(*n* = 55) 66.7	(*n* = 144) 73.7	0.627
Insulin resistance‖	773	(*n* = 403) 1.4	(*n* = 197) 1.7	(*n* = 173) 2.3*#	<0.001	180	(*n* = 33) 2.9	(*n* = 56) 2.6	(*n* = 145) 2.9	0.421
Serum cholesterol (mg/dL)	1,074	172 ± 37	178 ± 35	186 ± 40*	<0.001	299	192 ± 42	197 ± 33	191 ± 37	0.535
Serum triglycerides (mg/dL)	1,074	105 ± 61	113 ± 53	137 ± 85*#	<0.001	299	124 ± 74	147 ± 83	146 ± 81	0.194
HDL cholesterol (mg/dL)	1,074	44 ± 10	42 ± 9	42 ± 10	0.05	299	45 ± 15	42 ± 10	42 ± 10	0.204
Positive family history of diabetes, *n* (%)	1,071	184 (31.1)	96 (34.7)	85 (41.9)	0.006	295	13 (25.0)	23 (32.4)	81 (47.1)†	0.002
Current smokers, *n* (%)	1,068	102 (17.3)	37 (13.5)	30 (14.6)	0.217	297	10 (19.2)	13 (18.3)	23 (13.2)	0.220
Current consumption of alcohol, *n* (%)	1,072	120 (20.4)	47 (17.1)	39 (18.7)	0.421	299	17 (32.7)	18 (25.4)	25 (14.2)†	0.002

Values are presented as mean ± SD for continuous variables and *n* (%) for proportions. DM, diabetes. *$P < 0.05$ compared with individuals who remained as NGT; #$P < 0.05$ compared with those who progressed to prediabetes; †$P < 0.05$ compared with individuals who regressed to NGT; ‡$P < 0.05$ compared with those who remained as prediabetes; §log transformed; ‖square root transformed; 53 individuals who died and whose glycemic status could not be ascertained were excluded from the analysis.

Table 3—Predictors of incident diabetes, prediabetes, and dysglycemia in the study cohort

	Progression to diabetes (NGT to DM)	Progression to diabetes (IFG/IGT to DM)	Progression to prediabetes (NGT to IFG/IGT)	Progression to dysglycemia (NGT to DM/IFG/IGT)
Variables*	HR (95% CI) *P* value	HR (95% CI) *P* value	HR (95% CI) *P* value	HR (95% CI) *P* value
Age (years)†	1.01 (1.00–1.03) *P* = 0.095	1.01 (0.99–1.03) *P* = 0.239	1.02 (1.00–1.03) *P* = 0.007	1.02 (1.01–1.03) *P* < 0.001
Sex (female)	1.01 (0.67–1.53) *P* = 0.954	1.10 (0.68–1.80) *P* = 0.691	0.77 (0.52–1.13) *P* = 0.184	0.88 (0.66–1.17) *P* = 0.375
Positive family history of diabetes	1.74 (1.24–2.45) *P* = 0.001	1.63 (1.10–2.42) *P* = 0.016	1.25 (0.91–1.72) *P* = 0.165	1.49 (1.18–1.87) *P* = 0.001
Abdominal obesity	1.03 (0.99–1.08) *P* = 0.124	0.99 (0.93–1.05) *P* = 0.698	1.32 (0.96–1.80) *P* = 0.085	1.03 (1.00–1.05) *P* = 0.039
2-h PG (mg/dL)†	1.01 (1.00–1.02) *P* = 0.012	1.01 (1.00–1.01) *P* = 0.086	1.01 (1.00–1.02) *P* = 0.005	1.01 (1.01–1.02) *P* < 0.001
HbA_{1c} (%)†	3.25 (2.24–4.72) *P* < 0.001	1.61 (1.23–2.11) *P* = 0.001	0.96 (0.69–1.33) *P* = 0.809	1.04 (1.01–1.07) *P* = 0.003
HOMA-IR†	1.04 (0.94–1.16) *P* = 0.447	1.04 (0.95–1.15) *P* = 0.395	0.99 (0.97–1.00) *P* = 0.041	0.97 (0.90–1.05) *P* = 0.511
High serum triglycerides	1.61 (1.14–2.27) *P* = 0.007	1.13 (0.75–1.71) *P* = 0.561	0.84 (0.57–1.25) *P* = 0.399	1.19 (0.92–1.54) *P* = 0.178
Low HDL cholesterol	1.33 (0.93–1.91) *P* = 0.117	1.24 (0.84–1.83) *P* = 0.286	1.35 (0.98–1.86) *P* = 0.068	1.34 (1.06–1.70) *P* = 0.016
Physical inactivity	1.38 (0.90–2.11) *P* = 0.137	1.43 (0.97–2.10) *P* = 0.070	1.94 (1.30–2.89) *P* = 0.001	1.66 (1.24–2.21) *P* = 0.001
Smoking (yes)	0.99 (0.54–1.81) *P* = 0.979	1.04 (0.53–2.02) *P* = 0.914	0.70 (0.37–1.32) *P* = 0.266	0.82 (0.53–1.26) *P* = 0.369
Alcohol (yes)	1.94 (1.08–3.47) *P* = 0.026	0.68 (0.34–1.34) *P* = 0.260	0.98 (0.54–1.77) *P* = 0.934	1.32 (0.88–1.99) *P* = 0.180

Abdominal obesity defined as waist circumference ≥80 cm for males and ≥90 cm for females. High serum triglycerides defined as serum triglycerides ≥150 mg/dL, and low HDL cholesterol defined as HDL cholesterol <40 mg/dL for males and <50 mg/dL for females. DM, diabetes; HOMA-IR, HOMA of insulin resistance; HR, hazard ratio. *All variables added simultaneously into the models; †included in the model as continuous variables.

5.5–5.9% (36.6–41.0 mmol/mol) among those with baseline prediabetes (Supplementary Fig. 1*A* and *B*).

CONCLUSIONS

Our study provides the first population-based data on the incidence of diabetes and prediabetes as well as the predictors of progression from NGT to various stages of dysglycemia in the Asian Indian population.

The incidence rate of diabetes among individuals with prediabetes in our cohort was 78.9 per 1,000 person-years, which is one of the highest reported in a large ethnic group and is comparable to the rates reported in small, isolated, and homogenous populations such as the Pima Indians (87.3 per 1,000 person-years) (12), the Micronesian population of Nauru (62.8 per 1,000 person-years) (12), and Native Americans in the Strong Heart Study (66.1 per 1,000 person-years) (13), whereas studies in white Caucasians report much lower incidence rates (35.0–40.0 per 1,000 person-years) (11,12,14). Our population exhibits these high incidence rates of diabetes despite being younger and having much lower levels of BMI and waist circumference than the Pima, Micronesian, and Native American populations. Part of this could be explained by the high prevalence of family history of diabetes in our population. It also represents rapid epidemiological transition in our population. This study confirms that the progression from prediabetes to diabetes occurs much faster in Asian Indians than in other ethnic groups and confirms the observations made in earlier cross-sectional studies (15,16).

Our study reports the incidence of diabetes and prediabetes among individuals with baseline NGT to be 22.2 and 29.5 per 1,000 person-years, respectively. This figure is comparable with the results of a previous small study performed by our group in two selected residential colonies in Chennai, in whom the incidence rates of diabetes and prediabetes were 20.2 and 13.1 per 1,000 person-years, respectively (5). The lower incidence of prediabetes in the earlier study could be explained by the use of a higher cut point of 110 mg/dL (6.1 mmol/L) for the diagnosis of IFG. The few other studies available in the literature on the development of prediabetes and diabetes in individuals with NGT show much lower incidence rates in Caucasian, East Asian, and Iranian populations (14,17–20).

Whereas our results regarding the incidence of prediabetes are similar to those reported in the Caucasian cohort in the Inter99 study (14), they are much lower than those reported for the biracial Pathobiology of Prediabetes in a Biracial Cohort (POP-ABC) (21). This is probably because the latter study was restricted to offspring of parents with diabetes, with an inherently high risk

of progression to dysglycemia. Studies on Pima Indians have reported much higher rates of incident prediabetes (22).

Our findings raise the possibility of a more aggressive course of the underlying pathophysiological process of type 2 diabetes in the Asian Indian population. For decades it has been known that Asian Indians tend to have higher plasma levels of insulin (23) and greater insulin resistance compared with matched groups of Caucasians (24). More recently we have shown that β-cell dysfunction occurs very early in the natural history of type 2 diabetes in Asian Indians (25). This combination of increased insulin resistance with rapidly failing β-cells may explain the faster transition to dysglycemia noted in this population.

The conversion rate from prediabetes to diabetes varies based on the population characteristics and the definition used to define diabetes and prediabetes. In a meta-analysis of prospective studies (26), the annualized incidence rates of progression to diabetes in individuals with i-IGT (4–6%) or i-IFG (6–9%) were lower than in those with both IFG and IGT (15–19%). In our study, the corresponding rates are 6.8, 6.1, and 13.4%, respectively, which are comparable to those reported in earlier studies.

Our results show that advancing age, positive family history of diabetes, 2-h PG, HbA_{1c}, low HDL cholesterol, and physical inactivity predict progression from NGT to dysglycemia. Earlier studies have shown that 2-h PG independently predicts the risk of future diabetes (27). It is well known that plasma glucose levels in the prediabetes range identify individuals at high risk of progressing to diabetes. In this context, it is interesting to note that the incidence of diabetes in our cohort started increasing even at baseline 2-h PG values well below the levels diagnostic of prediabetes. Also, our results show that the factors that lead to progression from NGT to dysglycemia varied somewhat from those predicting progression to diabetes. Physical inactivity and low HDL cholesterol predicted the development of prediabetes (but not diabetes) in those with NGT. Conversely, a positive family history of diabetes predicted the development of diabetes (but not of prediabetes) in those with NGT. Thus, it is tempting to speculate that whereas the development of prediabetes is linked to environmental factors such as physical inactivity, the subsequent development of diabetes is perhaps governed by a combination of genetic and environmental factors. Therefore, it appears reasonable to suggest that in this population, efforts to prevent diabetes would have to be initiated prior to the development of prediabetes in order to obtain the most benefit.

The strengths of the study are the representativeness of the sample and long duration of follow-up. The separation of prediabetic states into i-IGT, i-IFG, and combined IGT + IFG, enabling assessment of progression and its predictors separately, and in combination, for each of these entities, is another unique feature of the study. The limitations include lack of year-by-year follow-up data and dependence on self-report for diagnosis of diabetes in many cases. However, each such case was checked against available medical records to ensure accuracy of the diagnosis. The relatively low response rate is another limitation, although there were no significant differences with respect to the baseline demographic, anthropometric, or biochemical parameters between the 2,944 responders and the 645 nonresponders (Supplementary Table 1). Finally, as our study was conducted in a single urban city in southern India, the results need to be applied with caution before they can be generalized to the rest of the country as risk factors, prevalence, and progression to diabetes may well differ in rural areas of India.

Our results have important public health implications. The high rates of diabetes incidence obtained in our population give cause for concern, if only on account of the huge population of India, which is currently over 1.2 billion people in addition to several million Indians who live abroad. Thus our findings are of interest not only to clinicians and public health workers in India but also to those in the U.S., Europe, and other parts of the globe (e.g., Fiji, South Africa, Mauritius, Singapore, Malaysia, and Sri Lanka) that are home to large populations of Asian Indian ethnicity. Awareness of the predictors of incident diabetes will help in the identification of individuals at highest risk so that appropriate preventive measures could be taken to slow down the epidemic of diabetes in this population.

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Author Contributions. R.M.A. and V.M. conceived the study and its design, were involved in implementation of the study and interpretation of the data, and helped draft and revise the manuscript. C.S.S.R. and M.D. were involved in the design and coordination of the study, interpretation of the data, and drafting the manuscript; helped in the execution of the study; and were responsible for maintaining quality. R.P., V.S., and R.U. were involved in the interpretation of the data and drafting the manuscript. H.D.N., N.L., and S.S. were responsible for data management and statistical analysis. V.S.B. provided statistical guidance and support. All authors read and approved the final manuscript. R.M.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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