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C O N T E N T S

Identification of the risk factors for the high prevalence of type 2 diabetes and its complications in a Punjabi population: North Indian Diabetes Study: A case-control study

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AIM: The incidence and prevalence of type 2 diabetes mellitus (T2DM) is rising at alarming rates in India. The North Indian Diabetes Study was launched to investigate the relative contributions of the risk factors to the susceptibility to T2DM among the Punjabi population in North India. **METHODOLOGY:** In this study, 563 T2DM patients (313 male, 250 female) and 413 nondiabetic controls (189 male and 224 female) were recruited from North India. A standardized questionnaire was used to collect information about age, onset of diabetes, sex, smoking, alcohol, diet, physical activity, migration history, household information and family history of diabetes. Standard anthropometric measurements including height, weight and waist and hip circumferences were performed. All individuals were clinically diagnosed using standard procedures and information on medication use and associated diabetic complications was compiled. **RESULTS:** The mean age of diagnosis of T2DM was 48.6 ± 10.3 years. The average duration of diabetes was longer in males than in females (8.9 ± 0.7 *vs.* 6.9 ± 0.8 years; $P < 0.05$). The mean BMI values did not vary among diabetic and nondiabetic subjects (27.4 ± 4.7 *vs.* 26.9 ± 4.5; $P = 0.172$) but female diabetics had significantly higher BMI. Patients had pronounced abdominal adiposity, which was reflected by their significantly higher waist circumference (37.0 ± 4.3 in patients *vs.* 35.2 ± 4.3 in controls; $P = 0.000$) and higher waist-to-hip ratio (WHR) (0.97 ± 0.07 in patients *vs.* 0.94 ± 0.08 in controls; $P = 0.000$). Insulin resistance syndrome (HOMA-IR) with low levels of HDL-C and high levels of TG, VLDL-C and HbA_{1c} were observed in T2DM cases as compared with controls ($P < 0.05$). Diabetic complications were significantly higher in T2DM subjects than in controls (CHD: 18% *vs.* 9.7%; hypertension: 61.3% *vs.* 38%; neuropathy: 52.3% *vs.* 31.1%; and ocular complications: 43.8% *vs.* 32.7%). **CONCLUSIONS:** This study documents that the North Indian Punjabi population is at high risk for developing diabetes and its complications in comparison with other Asian communities which, in part, is contributed to by morphological/biological attributes like physical inactivity, upper-body adiposity (as assessed by the WHR), body fat percent, dyslipidemia and insulin resistance (HOMA-IR).

KEY WORDS: Abdominal obesity, insulin resistance, North Indians, Punjabi population, type 2 diabetes

Introduction

Type 2 diabetes mellitus (T2DM) has become a major public health problem and, across the world, is associated with enormous personal, social and economic burden. The worldwide prevalence of diabetes, for all age groups, was estimated to be 2.8% in 2000 and is predicted to be 4.4% in 2030.[1] India is expected to experience the largest increase in T2DM by the year 2030. Diabetes in urban Indians is reaching an epidemic scale.[2-7] The prevalence of T2DM in Asian Indians ranges from 2.7% in rural India to 14% in urban India and up to 16-22% in migrant Indians living in Europe, USA, Africa, and Fiji.[8-11] This increase is of great concern because of the high morbidity and mortality and the cost associated with the treatment of the complications

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of diabetes.[12,13] Recently, a family-based study conducted in North India indicated the high susceptibility to T2DM and its related complications in the Khatri Sikh population.[14] T2DM is a multifactorial disease, with both genetic and environmental factors contributing to its development.[15] Many risk factors have been identified which influence the prevalence of T2DM.[16] Factors of particular importance are: family history of diabetes, age, obesity, increased abdominal fat, hypertension, ethnic background and lack of physical exercise. Several biochemical parameters have also been identified as risk factors, including fasting hyperinsulinemia, decreased HDL-C and increased triglycerides and LDL-C levels.[17] T2DM exhibits familial predisposition, indicating strong genetic components associated with the susceptibility to the disease. Various studies on the prevalence and risk factors associated with T2DM have been carried out in India in the past but most of them have been confined to South Indian populations. A few authenticated reports have been published on the population residing in New Delhi[4,6,7,18] and Kashmir.[19] However, scarcely any information is available on the prevalence and risk factors associated with T2DM in the North Indian Punjabi population. The main aim of this study is to investigate risk factors associated with the pathogenesis of T2DM in the Punjabi population of North India.

Methodology

The study sample included 976 individuals (563 T2DM and 413 nondiabetic unrelated controls) from urban areas of Punjab and Chandigarh. The study was advertised region wise and T2DM patients and nondiabetic controls were invited to participate at the designated recruitment centers. Handicapped or elderly patients were also recruited from their homes. The diagnosis of T2DM was done, using criteria established by the American Diabetes Association,[20] i.e.: a medical record indicating either a fasting plasma glucose (FPG) level ≥ 7.0 mmol/l or ≥ 126 mg/dl after a minimum 12-h fast, or a 2-h post-glucose level (oral glucose tolerance test or 2-h OGTT) ≥ 11.1 mmol/l or ≥ 200 mg/dl on more than one occasion, with symptoms of diabetes. Impaired glucose tolerance (IGT) was defined as an FPG level of 100 mg/dl (5.6 mmol/l) but < 126 mg/dl (7.0 mmol/l) or 2-h OGTT of ≥ 140 mg/dl (7.8 mmol/l) but < 200 mg/dl (11.1 mmol/l). The diagnosis of T2DM was based on clinical records and medication. In the absence of information from medical records, we confirmed a self-reported T2DM case by establishing that there is regular treatment with hypoglycemic medication or by performing a 2-h OGTT. The study was approved by the ethical committees of the participating hospitals and Panjab University, Chandigarh. Informed written consent was obtained from all the subjects.

Clinical and biochemical measurements

All anthropometric measurements, including height, weight, waist and hip circumferences and blood pressure were measured using standardized procedures. Body mass index (BMI) was calculated as [weight (kg)/height $(m)^2$]. BMI values were defined according to the recent recommendations of WHO for Asians.[21] Abdominal obesity was diagnosed according to the new cut-offs proposed for South Asian Indians[22] [i.e., waist-to-hip ratio (WHR) > 0.89 for men and > 0.81 for women]. Hypertension was defined by systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg or a history of taking antihypertensive medication. Overnight fasting blood samples were taken in EDTA disodium-coated and plain vials and centrifuged to obtain plasma, serum and buffy coat, which was stored at −80°C. Total cholesterol (TC), triglycerides (TG) and HDL-C levels were estimated in serum, using kits (Merck, Germany). LDL-C was calculated using the Friedewald formula:[23] LDL-C = TC – [HDL-C – (TG in mg/dl/5)]. Insulin level was measured in the serum by chemiluminescence immunoassay. Glycosylated hemoglobin (HbA_{1c}) was measured in the whole blood by reflectometry. Fasting blood glucose level was measured in whole blood using One Touch Ultra glucometer (Johanson and Johanson, USA). All the quantitative parameters were measured by following the manufacturers' instructions, using Hitachi-912 (Hitachi, Germany) and Metrolab 2300 (Metrolab, USA) autoanalyzers.

Homeostasis model assessment (HOMA) index

The insulin resistance indices HOMA-IR and HOMA-BF were used to evaluate insulin resistance and beta-cell functions, respectively,[24] using the following formulae:

Insulin resistance (HOMA-IR) = [fasting insulin (μU/ml) × fasting blood glucose (mmol/l)]/22.5 and

Beta-cell function (HOMA-BF) = [20 × fasting insulin (μU/ml)]/fasting blood glucose (mmol/l).

Body fat percentage was calculated according to the method of Lean *et al.*,[17] using the following formulae:

Body fat % for men = [(0.567 × waist circumference in cm) + (0.101 × age in years)] – 31.8; and

Body fat % for women = [(0.438 × waist circumference in cm) + (0.221 × age in years)] – 9.4

Statistical analysis

Data are presented as mean ± SD. Analyses were performed using SPSS (version 11.5). Group means were compared using one-way ANOVA or the unpaired '*t*' test. Univariate and linear regression analysis were performed for determining the relationship between the disease (T2DM) and the other variables and Pearson correlation coefficient was obtained. Data were also analyzed by multiple linear regression, using T2DM as the dependent variable (stepwise forward method). Independent variables, including BMI, waist, body fat percent, HOMA-IR and HOMA-BF were forced into the model. A *P*-value of less than 0.05 was considered as statistically significant.

Results

The demographic and socioeconomic characteristics of the participants are summarized in Table 1. There are no significant differences between diabetic patients and controls in respect of economic status, education, and diet. Of the 563 T2DM patients, 8.2% were maintaining glycemic control with diet and exercise, 68.3% were taking oral hypoglycemic agents, 3% were on insulin therapy, 7.45% were on insulin treatment along with oral agents, and 12% were not taking any regular treatment. During this study, 31 individuals were newly diagnosed T2DM patients. Alcohol intake was significantly higher and physical activity was significantly lower in diabetic subjects than in the controls. Unlike Western populations, the frequency of non-vegetarian food intake among the North Indian Diabetes Study (NIDS) subjects, in general, was very low (once a week or once a month), with the exception of <2% of individuals who were regularly having a non-vegetarian diet. Age-specific prevalence of T2DM is shown in Figure 1. The present data shows that the prevalence of T2DM increases with age, especially after 40 years, and reaches a maximum at 50-60 years of age. Logistic regression analysis of the data revealed that our population has the strongest age-associated risk for diabetes among all the groups.

Table 2 describes the anthropometric and biochemical characteristics of the NIDS subjects. The mean age of diagnosis of T2DM was 48.4 ± 10.7 years for male and 48.9 ± 9.9 years for female diabetic subjects. The average duration of diabetes was longer in males than in females. The mean BMI values did not differ significantly among

Table 1: The demographic and socioeconomic characteristics of the North Indian Diabetes Study participants

Characteristics		Type 2 diabetic patients (%)			Controls (%)		
		Male (*n* = 313)	Female (*n* = 250)	Total (*n* = 563)	Male (*n* = 189)	Female (*n* = 224)	Total (*n* = 413)
Economic status	High-income class	28.1	13.2	21.49	27.0	15.2	20.6
	Middle class	57.8	75.6	66.7	56.6	71.4	64.6
	Low-income class	14.1	10.4	12.25	16.4	13.4	14.8
Education	Illiterate	3.8	10.8	7.3	3.7	10.7	7.2
	Elementary	12.8	22	17.4	7.4	14.7	11.05
	High school	41.5	35.2	38.35	39.2	32.2	35.7
	Diploma	5.8	6	5.9	7.9	6.7	7.3
	University degree	36.1	26	31.05	41.8	31.7	36.75
Alcohol consumption	Teetotalers	62.9	100	81.45	71.4	99.6	85.5
	Moderate	16.3	0	8.15	10.6	0	5.5
	Heavy	11	0	5.5	12.2	0	6.1
	Very heavy	8.9	0	4.45	5.8	0	2.9
Cooking media	Desi ghee (melted butter)	9.3	5.2	7.25	6.3	8	7.15
	Refined oil	65.8	73.2	69.5	72.5	68.3	70.4
	Mustard oil	11.5	9.2	10.35	7.9	9.8	8.85
	Dalda ghee (hydrogenated oil)	4.8	4.8	4.8	6.3	5.4	5.85
	Mixed	8.6	7.6	8.1	6.9	8.5	7.7
Eating habits	Vegetarians	43.5	67.2	55.35	46.6	59.8	53.2
	Nonvegetarians	56.5	32.8	44.65	53.4	40.2	46.8
Physical activity	Very active	26.2	16.4	21.3	36	27.2	31.6
	Moderately active	70	74.4	72.2	61.9	68.3	65.1
	Sedentary	3.8	9.2	6.5	2.1	4.5	3.3

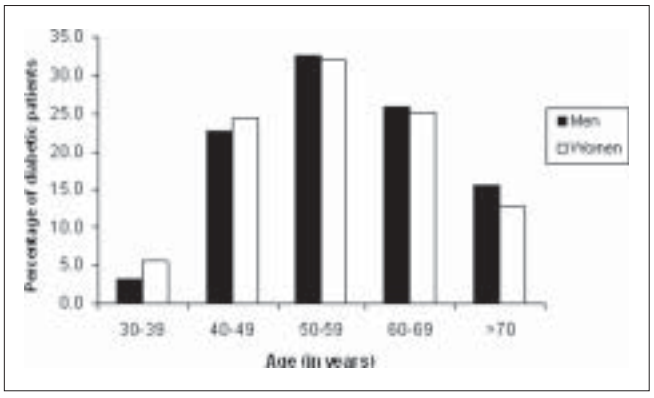

Figure 1: Percentage of diabetic patients at each decade

diabetic and control subjects (27.4 ± 4.7 *vs.* 26.9 ± 4.5; $P = 0.172$) but significantly higher BMI was observed in female diabetic subjects (26.4 ± 4.0 for males *vs.* 28.5 ± 5.2 for females; $P < 0.05$). However, despite non-obese BMI, patients had a pronounced abdominal adiposity as evidenced by their significantly higher waist circumferences (37.0 ± 4.3 in patients *vs.* 35.2 ± 4.3 in controls; $P = 0.000$) and higher WHR (0.97 ± 0.07 in patients *vs.* 0.94 ± 0.08 in controls; $P = 0.000$). Following stratification of the NIDS data, based on the new BMI cut-offs advised by WHO Expert Consultation,[18] we observed pronounced central obesity (as assessed by WHR) in both patients and controls even at the lowest BMI values (<23 kg/m^2).

We have calculated body fat content (%) using the formula involving age and waist circumference [Table 2]. It has been observed that female diabetic patients have significantly higher body fat content compared to male patients. Similarly, in the controls, female subjects have significantly higher body fat content than male subjects. However, diabetic subjects did not exhibit significant increase in body fat percent compared to normal subjects. (34.4 ± 9.8 *vs.* 33.3 ± 9.1; $P = 0.077$). Significantly higher values of blood pressure (systolic and diastolic) were observed in diabetics compared to controls.

The biochemical parameters in the NIDS subjects are summarized in Table 2. There was a significant difference observed in fasting TG (177.78 ± 98.2 *vs.* 158.4 ± 77.6; $P = 0.019$), HDL-C (39.6 ± 12.6 *vs.* 41.5 ± 10.9; $P = 0.05$), HbA_{1c} (10.7 ± 6.7 *vs.* 8.2 ± 3.4; $P = 0.00$), and insulin levels (8.65 ± 2.4 *vs.* 6.71 ± 1.7; $P = 0.00$) between diabetic and nondiabetic subjects. The diabetic patients had hyperglycemia and were not in good metabolic

Table 2: Anthropometric and biochemical characteristics of the study subjects by sex and disease status

Variables	Type 2 diabetic patients			Controls			*P*
	Male (*n* = 313)	Female (*n* = 250)	Total (*n* = 563)	Male (*n* = 189)	Female (*n* = 224)	Total (*n* = 413)	
Age (years)	57.3 ± 10.4	55.8 ± 10.6	56.7 ± 10.5	53.9 ± 15.6	52.3 ± 13.4	53.0 ± 14.5	0.000
Onset of T2DM (years)	48.4 ± 10.7	48.9 ± 9.9	48.6 ± 10.3	-	-	-	
Duration of T2DM (years)	8.9 ± 7.2	6.9 ± 6.0[a]	8.09 ± 6.7	-	-	-	
BMI (kg/m^2)	26.4 ± 4.0	28.5 ± 5.2[a]	27.4 ± 4.7	26.6 ± 4.0	27.3 ± 5.0	26.9 ± 4.5	0.172
Waist (inches)	37.3 ± 4.0	36.7 ± 4.6	37.0 ± 4.3	36.4 ± 4.1	34.1 ± 4.2[b]	35.2 ± 4.3	0.000
Hip (inches)	37.6 ± 3.3	39.0 ± 4.4[a]	38.2 ± 3.9	37.4 ± 2.8	37.6 ± 3.7	37.5 ± 3.3	0.004
WHR	0.99 ± 0.07	0.94 ± 0.06[a]	0.97 ± 0.07	0.97 ± 0.06	0.91 ± 0.07[b]	0.94 ± 0.08	0.000
Body fat (%)	27.2 ± 5.7	43.4 ± 5.4[a]	34.4 ± 9.8	25.7 ± 5.8	39.7 ± 5.9[b]	33.3 ± 9.1	0.077
Systolic BP (mmHg)	149 ± 22.6	150 ± 24.4	149 ± 23.4	141.5 ± 23.8	137 ± 25.8[b]	139 ± 25.0	0.000
Diastolic BP (mmHg)	85.5 ± 12.1	85.6 ± 11.6	85.5 ± 11.9	84.3 ± 12.7	80.6 ± 14.5[b]	82.3 ± 13.8	0.000
Glucose (mg/dl)	188.2 ± 65.2	187.5 ± 66.4	187.9 ± 65.7	96.4 ± 8.70	96.5 ± 8.7	96.5 ± 8.73	0.000
TC (mg/dl)	186.2 ± 48.1	193.4 ± 45.5	189.1 ± 47.1	186.2 ± 48.5	179.7 ± 36.1	182.5 ± 41.9	0.109
TG (mg/dl)	178.5 ± 99.5	176.6 ± 96.5	177.8 ± 98.2	168.9 ± 76.6	150.3 ± 77.8	158.4 ± 77.6	0.019
HDL-C (mg/dl)	38.5 ± 12.2	41.2 ± 13.1[c]	39.6 ± 12.6	40.2 ± 11.1	42.9 ± 10.6	41.5 ± 10.9	0.052
LDL-C (mg/dl)	111.9 ± 46.8	116.8 ± 39.7	113.9 ± 44.2	112.3 ± 47.0	106.7 ± 35.4	109.2 ± 40.9	0.217
VLDL-C (mg/dl)	35.7 ± 19.9	35.3 ± 20.1	35.6 ± 19.5	33.8 ± 15.3	30.1 ± 15.6	31.7 ± 15.5	0.019
Creatinine (mg/dl)	0.97 ± 0.5	0.77 ± 0.3[d]	0.89 ± 0.43	0.93 ± 0.20	0.77 ± 0.2[e]	0.84 ± 0.2	0.116
Insulin (IU/ml)	10.7 ± 4.4	10.7 ± 7.2	10.7 ± 6.7	8.12 ± 3.5	8.3 ± 3.3	8.2 ± 3.4	0.000
HbA_{1c} (%)	8.58 ± 2.4	8.75 ± 2.4	8.65 ± 2.4	6.85 ± 1.7	6.59 ± 1.7	6.71 ± 1.7	0.000
HOMA-IR	4.75 ± 3.4	4.85 ± 3.5	4.79 ± 3.4	2.01 ± 0.9	2.05 ± 0.9	2.03 ± 0.8	0.000
HOMA-BF	44.3 ± 41.0	41.8 ± 37.3	43.3 ± 39.5	81.9 ± 35.2	85.9 ± 38.4	84.2 ± 36.9	0.000

Values are expressed as mean ± SD. *P*-values represent the difference between type 2 diabetic patients and nondiabetic controls; [a]Significant difference between male and female diabetic patients; [b]Significant difference between male and female nondiabetic control subjects; [c]Significant difference between male and female diabetic patients; [d]Significant difference between male and female nondiabetic control subjects ($P = 0.000$); [e]Significant difference between male and female nondiabetic control subjects ($P = 0.000$)

control. Indices of insulin sensitivity (HOMA-IR) and insulin secretion (HOMA-BF) were similar in men and women. As expected, diabetic subjects had higher insulin resistance (as seen from the high HOMA-IR values) than controls (4.79 ± 3.4 *vs.* 2.03 ± 1.8; $P = 0.000$). About 87% of diabetic subjects and 42.3% of controls showed evidence of insulin resistance (HOMA-IR > 1.93). In addition, the values of HOMA-BF in diabetic subjects were significantly lower than that in normal subjects (43.3 ± 39.5 *vs.* 84.2 ± 36.9; $P = 0.000$), indicating defective pancreatic function. Insulin resistance syndrome with a low level of HDL-C (<40 mg/dl in men and <50 mg/dl in women) was observed in diabetic subjects but not in controls.

The data on diabetes-related complications are summarized in Table 3. Of all the diabetic subjects in this study, 18% had clinically diagnosed CHD, 4.7% had had a paralytic stroke, and 43.8% had ocular complications (e.g., cataracts, retinal problems, glaucoma, hemorrhages and vision loss). About 52.3% of affected individuals suffered from peripheral or autonomic neuropathy and 28.3% had frequent non-healing skin and soft tissue infections or ulcers of the leg or foot. Significantly higher frequencies of diabetes-related complications (hypertension, cardiovascular disease, neuropathy, retinopathy and infections) were observed in the NIDS subjects. Despite the high frequency of hypertension observed (61.3%), only 4.7% of the NIDS patients had renal disease or kidney-related complications. No significant differences were observed in the frequencies of nephropathy, stroke and psychiatric and dental disorders between patients and controls.

From Table 4 and Figure 1 it can be seen that as the age increases (40 years onward), the risk of developing T2DM also increases. Subjects having a family history of diabetes were at the highest risk in their productive years of life. Insulin resistance (HOMA-IR) may be the greatest risk factor for the development of T2DM in our population as it increases the risk about 6-fold. The results of multiple logistic regression analyses of the data shows significant associations of T2DM with waist circumference (OR = 1.64 (95% CI: 1.17-2.30); $P = 0.00$), WHR (OR = 2.9 (95% CI: 1.7-5.0); $P = 0.00$), and triglycerides (OR = 1.46 (95% CI: 1.02-2.09); $P = 0.04$). However, no significant association was observed with BMI (OR = 1.2 (95% CI: 0.9-1.7); $P = 0.17$). Family history of diabetes may also play a major role in the pathogenesis of T2DM (OR = 4.1 (95% CI: 2.8-5.9); $P = 0.00$) in the North Indian Punjabi population.

Discussion

The present case-control study was undertaken to establish the risk factors associated with T2DM in the Punjabi population of North India. Asian Indians have been identified as one of the ethnic groups with a high prevalence[4,7] and familial aggregation of T2DM.[25] About 80% of the diabetic subjects have one or both parents affected, which shows high familial aggregation of T2DM in this North Indian population. The findings described in this paper confirm and extend our knowledge of the dynamics of the present epidemic of T2DM in North India. Many risk factors have been identified in Asian Indians,[16] but their conclusive role is still unclear.

Physical activity has an impact on many of the components of the metabolic syndrome. The rapid globalization and industrialization occurring in developing countries has produced much advancement on the social and economic front. These improved socio-economic conditions have resulted in a decrease

Table 3: Incidence of comorbidities among study population stratified by sex and disease status

Disease	Type 2 diabetes patients (%)			Nondiabetic controls (%)			*P*
	Male (*n* = 313)	Female (*n* = 250)	Total (*n* = 563)	Male (*n* = 189)	Female (*n* = 224)	Total (*n* = 413)	
Coronary heart disease	20.8	15.2[a]	18.0	12.7	6.7	9.7	0.000
Stroke	5.8	3.6	4.7	2.1	3.1	2.6	0.096
Hypertension	60.7	62.0	61.3	39.7	36.6	38.0	0.000
Ocular complications	43.1	44.4	43.8	32.3	33	32.7	0.001
Nephropathy	5.4	4.0	4.7	3.2	3.6	3.4	0.334
Neuropathy	47	57.6	52.3	22.8	39.3	31.1	0.000
Infections (skin and urinary)	23	33.6	28.3	11.6	14.6	13.1	0.000
Psychiatric disorder	12.1	11.6	11.8	7.9	8.9	8.4	0.091
Dental disorder	59.3	58.8	59.1	58.6	64.7	61.3	0.501

P-values represent the difference between type 2 diabetic patients and nondiabetic controls

Table 4: Multiple logistic regression analysis using T2DM as the dependent variable

Parameters		B	S.E.	Test of association	
				P	Odd ratio (95% C.I.)
Age (years)	30-39				1
	40-49	1.44	0.3	0.00	4.24 (2.52-7.13)
	50-59	2.04	0.3	0.00	7.67 (4.55-12.94)
	60-69	1.92	0.3	0.00	6.81 (4.00-11.61)
	>69	1.50	0.3	0.00	4.50 (2.57-7.88)
Physical activity	Very active				1
	Moderately active	0.45	0.1	0.00	1.57 (1.18-2.10)
	Sedentary life	0.96	0.3	0.00	2.62 (1.35-5.11)
Body mass index (kg/m^2)	Normal (<23)				1
	Overweight (>23-27.5)	0.30	0.18	0.09	1.37 (0.95-1.97)
	Obesity (>27.5)	0.10	0.18	0.48	1.14 (0.80-1.63)
Abdominal obesity	Waist circumference	0.50	0.2	0.00	1.64 (1.17-2.30)
Triglycerides	0.38	0.18	0.04	1.46 (1.02-2.09)	
HDL-C	0.03	0.19	0.87	1.03 (0.71-1.50)	
Family history of diabetes	1.59	0.2	0.00	4.92 (3.42-7.08)	
HOMA-IR	1.75	0.21	0.00	5.73 (3.78-8.69)	

in physical activity and an increase in obesity, which has led to the increase in the prevalence of T2DM and its related complications in Asian Indians. The data from this study suggests that those leading a sedentary lifestyle or involved only in household work develop diabetes more frequently than those whose occupation or routine life involved more physical work. South Asians and Asian Indians have been consistently shown to be less physically active when compared with other ethnic groups.[26-28] Moreover, increased intake of high-energy foods and an increase in psychosocial stress have proportionally increased the risk of disease even in relatively young adults between 25 and 35 years of age.

We have observed that the age-standardized prevalence of diabetes and its complications are high in both men and women. Our findings revealed that the NIDS subjects develop T2DM in their most productive years of age. The exact age of onset of T2DM subjects is not clear because many individuals in this population do not undergo regular checkups until symptoms appear; thus, diabetes may remain undiagnosed for 4 to 7 years.[29] Studies in India and abroad have shown that Indians develop diabetes at relatively young ages at least 10-15 years earlier than the white population.[30,31] Various studies carried out in India have shown that more than 50% of patients with diabetes developed the disorder before the age of 50 years.[4,7,30]

Our population presents an unusual clinical picture of uneven distribution of adiposity and high rates of diabetes. Although BMI has not been shown to be a significant risk factor in our population, their values were comparatively higher than that seen in South Indian populations. The data shown in Table 2 indicates a strong tendency toward upper-body adiposity (increased waist circumference and WHR) even in the control groups. Abdominal obesity might be a strong factor for the high frequency of insulin resistance and the subsequent metabolic complications in our population. Even small increments in body weight produce adverse changes in insulin sensitivity and in blood glucose levels. A recent study[4] has shown that the prevalence of upper-body adiposity was more than 'overweight' as indicated by BMI ≥ 25 kg/m^2 (30.8%). Studies in India have shown also that central obesity was more strongly associated with glucose intolerance than generalized obesity.[3,32] Lean Asian Indians have values of WHR similar to that seen in Mexican Americans with higher BMI.[33] In other words, Asian Indians have a higher degree of central adiposity for a given BMI. This might be due to a predisposition to deposit abdominal fat. Studies carried out in UK[34] and in USA[11,35,36] have suggested that Asian Indians had insulin resistance despite having non-obese BMI and that this could reflect the presence of a high percentage of visceral fat. McKeigue *et al*.[34] reported that every 0.04 unit increase in WHR was associated with a 4-fold increase in diabetes, 2-fold higher post-glucose insulin levels and significantly higher TG and lower HDL. The higher prevalence of diabetes in Asian Indians, compared with Europeans might be partly

related to abdominal obesity. Asian Indians have a greater amount of intra-abdominal fat[35,37] and thicker truncal skinfolds.[11,35,38]

Body fat percentage at a given BMI is comparatively higher in Asian Indians than in Chinese and Malays. A similar trend is observed in our population [Table 2]. Based on the new thresholds for Asian Indian BMI,[21] about 82% of our population falls above the healthy limits of BMI (23 kg/m^2) and are, therefore, at increased risk for developing fat-related illnesses. It has been suggested that thrifty genes that provided a survival advantage in previous eras now result in central obesity and T2DM in populations living in the rapidly modernizing environment of India.[34,39] A high proportion of upper-body fat or abdominal fat, independent of overall obesity, is recognized as an important component in the insulin resistance linked to obesity and T2DM.[37,40,41]

Dyslipidemia is defined by alterations in blood lipid levels. The significantly high levels of triglycerides and low levels of HDL-C observed in our population probably contribute to insulin resistance. About 53.7% males and 72% females have their HDL-C level below limits (<40 mg/dl in men and <50 mg/dl in women). Inter-ethnic comparison showed higher levels of serum triacylglycerols in adult Asian Indians,[42,43] which manifests at a young age.[38,43] Hypertriglyceridemia in Asian Indians was observed predominantly in people belonging to the high socio-economic strata[44,45] as compared with the low socioeconomic strata rural populations. Low HDL-C levels are also characteristically seen in Asian Indians.[43,46-48] Dyslipidemia along with abdominal obesity might contribute to insulin resistance which, in turn, results in increased prevalence of T2DM and its complications in this North Indian Punjabi population.

To conclude, in this study, we observed an early progression to diabetes which, in part, is due to the morphological/biologic attributes, such as upper-body adiposity (as indicated by a high WHR), body fat percent, physical inactivity, high triglycerides and HOMA-IR. Studies need to be conducted to determine whether a genetic predisposition can be one of the contributing factors in the pathogenesis of T2DM in this population.

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