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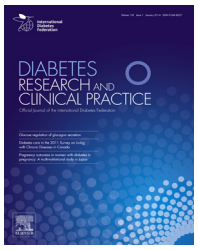

# Diabetes in Asian Indians—How much is preventable? Ten-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES-142)

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ABSTRACT

We sought to evaluate the contribution of various modifiable risk factors to the partial population attributable risk ($PAR_p$) for diabetes in an Asian Indian population. Of a cohort of 3589 individuals, representative of Chennai, India, followed up after a period of ten years, we analyzed data from 1376 individuals who were free of diabetes at baseline. A diet risk score was computed incorporating intake of refined cereals, fruits and vegetables, dairy products, and monounsaturated fatty acid. Abdominal obesity was found to contribute the most to incident diabetes [Relative Risk (RR) 1.63(95%CI 1.21–2.20)]; ($PAR_p$ 41.1% (95%CI 28.1–52.6)]. The risk for diabetes increased with increasing quartiles of the diet risk score [highest quartile RR 2.14(95% CI 1.26–3.63)] and time spent viewing television [(RR 1.84(95%CI 1.36–2.49] and sitting [(RR 2.09(95%CI 1.42–3.05)]. The combination of five risk factors (obesity, physical inactivity, unfavorable diet risk score, hypertriglyceridemia and low HDL cholesterol) could explain 80.7% of all incident diabetes (95%CI 53.8–92.7). Modifying these easily identifiable risk factors could therefore prevent the majority of cases of incident diabetes in the Asian Indian population. Translation of these findings into public health practice will go a long way in arresting the progress of the diabetes epidemic in this region.



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## 1. Introduction

The South East Asian region is home to nearly one-fifth of the world's population with diabetes. India, the largest country in this region, has more than 66 million people with diabetes, and this is expected to increase to 101 million by 2035 [1,2]. Efforts to prevent or minimize the burden of this epidemic are therefore of paramount importance.

Prevention of disease in a population entails a thorough knowledge of the nature and relative importance of various risk factors prevalent in the population. The population attributable risk (PAR) is a statistical tool designed to estimate the relative contribution of a particular risk factor (e.g. obesity) to an outcome (e.g. diabetes) in the population. The PAR associated with a risk factor is defined as the proportion of cases that could be (theoretically) prevented if that particular risk factor were eliminated in the population.

The few previous studies that have estimated the contribution of various risk factors to the PAR for diabetes have been restricted primarily to white Caucasians [3–5], and Persians (Iranians) [6] with limited applicability to the Asian Indian (South Asian) population, due to socio-economic, cultural and demographic differences between populations, as well as differences in the prevalence of risk factors and the increased ethnic susceptibility of Asian Indians to diabetes [7]. In this paper, for the first time, we evaluate the contribution of various modifiable risk factors to the PAR for diabetes in an Asian Indian population, using data from the ten-year follow-up of a large epidemiological survey, conducted on a representative population of the largest city in South India.

## 2. Methods

### 2.1. Study population

The study population comprised of individuals participating in the ten-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES). The detailed methodology of CURES has been published elsewhere [8]. Briefly, the baseline survey of CURES was performed between 2001 and 2003 on 26,001 individuals of both genders aged 20 years and above, representative of Chennai (population—4.7 million) the largest city in southern India. The sample size was calculated in accordance with the main objective of CURES, i.e., to assess the prevalence of diabetes and its complications. To get 1000 adults (≥20 yr) with diabetes, a sample size range of 16,000–24,000 was estimated with 95% CI and 0.5% error. Assuming a dropout rate of 10%, a total of 26,000 adults were recruited from 46 Corporation wards using the systematic sampling technique. Of these, all individuals with self-reported or newly diagnosed diabetes ($n = 1382$) and every 10th subject of the original 26,000 individuals who were surveyed ($n = 2207$) were invited for further detailed investigations as explained below. These 3589 individuals (1382 + 2207) formed the follow-up cohort that was re-surveyed in 2012–2013, ten years after the baseline survey [(median 8.9 years and 22,905 person years of follow-up) (Fig. 1)].

Out of the 3589 individuals in the CURES follow-up cohort, 534 had died (14.9%) and 645 were lost to follow-up (18%). Hence a total of 2410 individuals were re-surveyed with a follow-up response rate of 82%. Of these 2410 individuals, participants who had diabetes at baseline were excluded. Out of the 534 who had died (14.9%), verbal autopsy was available in 381 individuals. Out of this, 29 people who died and were known to have developed diabetes before death were included in the analysis. Of the remaining 352 individuals, 299 had a diagnosis of diabetes at baseline itself and were hence excluded from this analysis. For the remaining 53 we were unable to ascertain the glycemic status at the time of death and hence we have excluded them from the analysis. Thus the present analysis concerns 1376 individuals (11,629 person-years of follow-up) who were free of diabetes at baseline (Fig. 1). The study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines (World Medical Association, International Conference on Harmonisation). The study protocol was approved by the Institutional Ethics Committee of Madras Diabetes Research Foundation, and written informed consent was obtained from all the study participants.

### 2.2. Exposure assessment

At baseline, details pertaining to demography, socio-economic status, medical and family history of diabetes (considered as positive if either or both the parents had diabetes), physical activity, tobacco and alcohol use were elicited using a structured, pre-tested and validated interviewer-administered questionnaire. The questions on physical activity were used to assess frequency, intensity and duration of various activities in the work, transport and recreational domains, as well as sedentary behavior such as sitting and TV viewing. Dietary details were assessed using a validated meal-based semi-quantitative food frequency questionnaire (FFQ) [9], containing 222 common food items consumed in the three main meals and snacks. Individuals reported the usual frequency of consumption and serving size of various food items over the past year using appropriate visual aids. The average daily nutrient and food intake was computed using 'EpiNu' (Nutritional Epidemiology, Food and Nutrient database, Version 1.0, Chennai).

Height, weight, waist circumference and blood pressure were measured using standardized techniques [8,10], and body-mass index (BMI) calculated as weight in kilograms divided by height in meters squared. Biochemical analyses including fasting plasma glucose and lipids were performed in all individuals; in addition, plasma glucose estimation 2 h after a 75 g oral glucose load was performed in individuals without diabetes.

Biochemical analyses were done in a laboratory certified by the National Accreditation Board for testing and calibration Laboratories (NABL), New Delhi and the College of American Pathologists (CAP), on a Hitachi-912 Auto analyzer (Hitachi, 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). LDL cholesterol was calculated using the Friedewald equation [11]. The intra- and inter-observer coefficients of variation for the biochemical assays ranged from 3.1 to 7.6%.

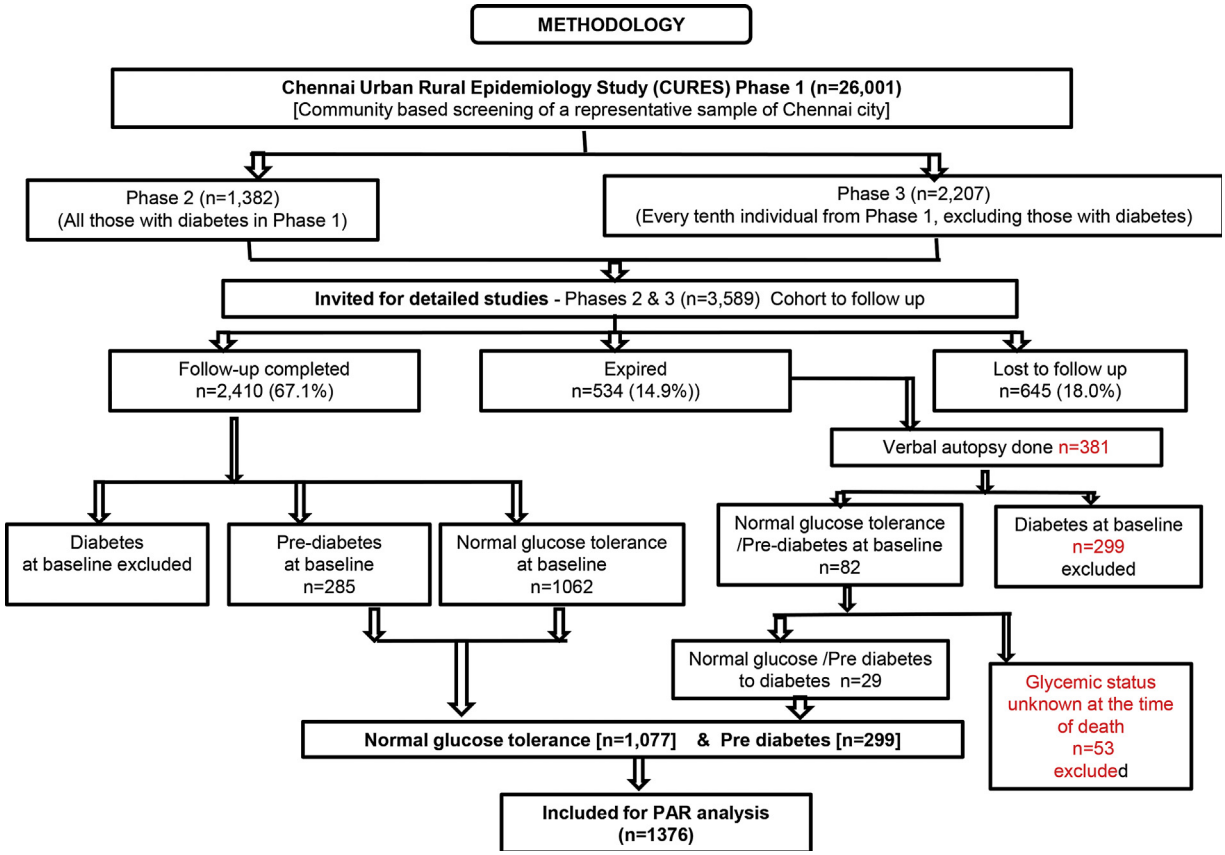


**Fig. 1 – Flow chart depicting study design.**

### 2.3. *Risk factor definitions*

Physical activity was dichotomously coded as active (moderate or vigorous intensity physical activity achieving at least 600 metabolic equivalent [MET]–minutes per week) or inactive (not meeting the above criteria) [13]. Total time spent in sitting and TV viewing was represented in quartiles of hours/day.

Generalized obesity was defined as BMI ≥23 kg/m$^2$ (including overweight specified for Asian Indians) based on World Health Organization (WHO) Asia Pacific guidelines. Abdominal obesity was defined as waist circumference ≥90 cm for men and ≥80 cm for women, based on World Health Organization (WHO) Asia Pacific guidelines [14]. Hypercholesterolemia was defined as total cholesterol levels ≥200 mg/dl (5.2 mmol/l), hypertriglyceridemia as serum triglyceride 1.7 ≥150 mg/dl (mmol/l), high LDL cholesterol as LDL cholesterol levels ≥100 mg/dl (2.6 mmol/l) and low HDL cholesterol, as HDL cholesterol levels <40 mg/dl (1.0 mmol/l) in men and <50 mg/dl (1.3 mmol/l) in women [15].

Refined cereals included white rice, rice grits-based products, rice flour, refined wheat flour, semolina and refined millet flour. Fruits and vegetables included all fruits and leafy and non-leafy vegetables and roots. Dairy products included milk, yoghurt and buttermilk.

### 2.4. *Outcomes assessment*

History of diabetes during the follow-up period was obtained through self-report and checked against medical records for validity. At the follow-up visit, a venous blood sample was drawn in the fasting state and 2 h after oral administration of 75 g of glucose to ascertain the diabetes status of all individuals who did not report a history of development of diabetes in the interim. Diabetes was diagnosed if the venous plasma glucose 2 h after oral glucose load was 11.1 mmol/l (≥200 mg/dl) and/or the fasting plasma glucose levels were 7.0 mmol/l (≥126 mg/dl) [12]. Information on death was obtained from members of the study participant's family. 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.

### 2.5. *Statistical analysis*

Statistical analyses were performed using SAS statistical package (version 9.2; SAS Institute, Inc., Cary, NC). Estimates were expressed as median (IQR) or proportions. Mann–Whitney *U* tests were used to compare differences between medians of continuous variables, and Chi-square tests were used to test differences in proportions. Those with glycemic status unknown at the time of death ($n = 53$) that could have potentially influenced the results (incidence of diabetes) were considered for sensitivity analysis. This showed no statistically significant difference between the missing and non-missing variables. In addition, invalid/missing data ($n = 42$) for

the variables of interest for estimating relative risks (RR) and PAR were also excluded. Potential variables with $p$ value <0.2 from the univariate analysis were considered and entered simultaneously into the multiple Poisson regression model. RR and 95% confidence intervals were obtained by introducing all the variables such as age (as a continuous variable), gender (male/female), family history of diabetes (yes/no), generalized obesity, abdominal obesity, hypertriglyceridemia, low HDL, household monthly income (<5000 INR[USD < 83]), physical inactivity (<600 MET min/week) into the Poisson regression model. Diabetes status at the end of follow-up was considered as the dependent variable in the regression. Follow-up time was calculated as the time between date of administration of baseline questionnaire and date of diagnosis of diabetes or date of last contact or death, whichever was earlier and was considered as an offset variable in the model. All the selected anthropometric, clinical and biochemical factors in the normal range measured at baseline were considered as low risk and taken as the reference group. $p$-Value < 0.05 was considered significant.

Dietary factors (food groups and macronutrients) associated significantly with incidence of diabetes were determined by multiple Poisson regression. Energy adjusted [16] higher intake of refined cereals and lower intake of fruits and vegetables, dairy and mono-unsaturated fatty acids (MUFA) were the dietary determinants that showed significant associations with diabetes risk These were therefore considered for the dietary risk score and partial PAR ($PAR_p$) analysis. For this analysis, we chose food groups, as these would be the easiest to translate for public health benefit. Although MUFA represents a macronutrient rather than a food group, its use in the analysis was necessitated by the low levels of consumption of MUFA-containing food sources such as nuts and seed oils in this population. The chosen dietary factors were categorized into quartiles of intake and the RR was estimated considering the lowest quartile as reference. All individuals were assigned a score of 1–4 corresponding to the quartile of intake of individual dietary items with 1 representing the optimal quartile and 4, the least desirable quartile. The quartile scores of all dietary factors were then summed and the total score was categorized further into quartiles. The lowest 25th percentile of the diet score was taken as the reference for calculation of RR and the 50th percentile, for PAR estimates.

Partial PAR and 95% confidence intervals for single modifiable factors as well as for combinations of factors adjusted for confounders were estimated for the overall cohort as well for either gender using the method described by Spiegelman [17]. PAR is said to be partial when one or more risk factors are considered to be eliminated while others are allowed to remain unchanged. In our analysis the fixed factors included age, family history of diabetes, house hold income and gender.

The following formula [17] was used to calculate the $PAR_p$.

$$PAR_P = \frac{\sum_{s=1}^{S}\sum_{t=1}^{T} p_{st}RR_{1s}RR_{2t} - \sum_{s=1}^{S}\sum_{t=1}^{T} p_{st}RR_{2t}}{\sum_{s=1}^{S}\sum_{t=1}^{T} p_{st}RR_{1s}RR_{2t}} = 1 - \frac{\sum_{t=1}^{T} p_{.t}RR_{2t}}{\sum_{s=1}^{S}\sum_{t=1}^{T} p_{st}RR_{1s}RR_{2t}}$$

In the formula mentioned above, $t$ denotes a stratum of distinct combinations of levels of all background risk factor ($t = 1, 2, 3,\ldots,T$) that are not considered in the study whereas $s$ indicates an index exposure group defined by each of the unique combinations of the levels of the index risk factors for which the $PAR_p$ applies ($s = 1,2, 3,\ldots,S$). $RR_{1s}$ is the relative risk analogous to combinations relative to the lowest risk combination, $RR_{1,1} = 1$. The combined prevalence of exposure group s and stratum t is designated by $_{Pst}$ and $P_{.t} = \sum_{s=1}^{S}$ [17].

## 3. Results

Among the 1376 individuals with 11,629 person-years of follow-up, there were 385 incident cases of diabetes.

Table 1 shows the baseline characteristics of the study population stratified by gender. Males were more likely to have family history of diabetes (males 39.1% vs. females 32.5%; $p = 0.012$) while females had a higher BMI [median (IQR)-Females 24.3(6.4) vs. males 22.8(6.0) kg/m$^2$; $p < 0.001$], 2-h plasma glucose[110(35) vs. 104(40) mg/dl; $p = 0.001$], serum total cholesterol [179(47) vs. 174(48) mg/dl; $p = 0.001$], HDL [45(12) vs. 38(12) mg/dl; $p < 0.001$] and LDL cholesterol [112 (40) vs. 108(39) mg/dl; $p = 0.028$] and were more likely to be physically inactive (85.2% vs.75.0%; $p < 0.001$) compared to males. A negligible proportion of females reported smoking and alcohol consumption, whereas among males, 38.1% reported smoking and 45.7% reported consuming alcohol; hence neither smoking nor alcohol were considered for further analysis.

Among the dietary variables, except for total energy intake [males—median(IQR) 2787(1064) vs. females 2352(902) kcal/day; $p < 0.001$)], % energy derived from carbohydrate [males—64 (8.0) vs. females 64.9 (8.0); $p = 0.005$] and trans-fats [males 0.04 (0.07) vs. females 0.03 (0.06); $p = 0.011$], there was no difference in the intake of any of the food groups and macronutrients between the genders (Table 2).

Table 3 shows the multiple Poisson regression model and $PAR_p$ for diabetes for various modifiable risk factors. Age (RR 1.04:95% CI 1.03–1.04), male gender (1.48:1.17–1.86), family history of diabetes (2.63:2.10–3.30), overweight and obesity (1.51: 1.13–2.03), abdominal obesity (1.63:1.21–2.20), hypertriglyceridemia (1.49:1.18–1.88), low HDL (1.37:1.07–1.75), physical inactivity (1.58:1.23–2.03) and household income (1.92: 1.48–2.48) were all independent risk predictors of diabetes after mutually adjusting for all the variables in the model and additionally for household income. Smoking and alcohol were reported mainly by men. We thus ran the Poisson regression model for the individual risk of smoking and alcohol with diabetes in men. We found the RR for smoking was 1.13 [95%CI 0.98–1.31; $p = 0.11$] and that of alcohol was 0.91 [95%CI 0.78–1.05; $p = 0.20$], after adjusting for age, BMI, waist, HbA1c, household income, energy adjusted protein and energy adjusted dietary fiber (g/d). The inverse RR and 95%CI did not allow the PAR macro to run this further and hence these variables were not considered for the PAR analysis. Among the individual contributions of the various modifiable risk factors, abdominal obesity was found to contribute the most to diabetes [$PAR_p$: 41.1% (95%CI: 28.1–52.6)], followed by generalized obesity [$PAR_p$: 37.4% (32.6–41.9)] and physical inactivity

**Table 1 – Baseline characteristics of the study population.**

| Variables | Overall $n = 1376$ | Male $n = 573$ | Female $n = 803$ | $p$ Value |
|---|---|---|---|---|
| Age (years) | 38.0 (17) | 38.0 (17) | 38.0 (18) | 0.976 |
| Positive family history of diabetes $n$ (%) | 482 (35.3) | 223 (39.1) | 259 (32.5) | 0.012 |
| BMI (kg/m$^2$) | 23.7 (6.3) | 22.8 (6.0) | 24.3 (6.4) | <0.001 |
| Generalized obesity (BMI > 23 kg/m$^2$) $n$ (%) | 768 (55.8) | 280 (49.1) | 488 (60.8) | <0.001 |
| Waist circumference (cm) | 85 (17.1) | 86.5 (17.8) | 84.0 (16.5) | 0.009 |
| Abdominal obesity (waist circumference: males ≥ 90 cm; females ≥ 80 cm) $n$ (%) | 729 (53.0) | 216 (37.7) | 513 (65.1) | <0.001 |
| Systolic BP (mm Hg) | 119 (21) | 119 (20) | 118 (23) | 0.490 |
| Diastolic BP (mm Hg) | 73 (13) | 73 (13) | 73 (13) | 0.251 |
| Fasting plasma glucose (mg/dl) | 85 (12) | 85.0 (12) | 85.0 (12) | 0.601 |
| 2 h plasma glucose (mg/dl) | 108 (38) | 104 (40) | 110 (35) | 0.001 |
| Glycated hemoglobin (%) | 5.6 (0.6) | 5.6 (0.6) | 5.6 (0.6) | 0.359 |
| Serum total cholesterol (mg/dl) | 176 (48) | 174 (48) | 179 (47) | 0.001 |
| Serum triglycerides (mg/dl) | 101 (67) | 107 (80) | 99 (61) | <0.001 |
| Hypertriglyceridemia (≥150 mg/dl) $n$ (%) | 300 (21.8) | 157 (27.4) | 143 (17.90) | <0.001 |
| HDL cholesterol (mg/dl) | 42 (13) | 38 (12) | 45 (12) | <0.001 |
| Low HDL (males <40 mg/dl; females <50 mg/dl) $n$ (%) | 939 (68.3) | 343 (60.6) | 596 (74.4) | <0.001 |
| LDL cholesterol (mg/dl) | 110 (40) | 108 (39) | 112 (40) | 0.028 |
| Current smokers $n$ (%) | 215 (15.8) | 214 (38.1) | 1 (0.1) | <0.001 |
| Current alcohol consumption $n$ (%) | 266 (19.4) | 260 (45.7) | 6 (0.7) | <0.001 |
| Household income (INR/month) <5000 (USD < 83) $n$ (%) | 1080 (78.5) | 429 (74.9) | 651 (81.1) | 0.006 |
| Physical inactivity $n$ (%) (<600 MET min/week) | 1099 (80.9) | 430 (75.0) | 669 (85.2) | <0.001 |

Median inter quartile range (IQR) in parentheses and statistical test was done by Mann–Whitney $U$ test for all variables. Chi-square used for categorical variable.

**Table 2 – Dietary intake reported by the study population.**

| Energy adjusted nutrients and food groups | Overall Median (IQR) | Male Median (IQR) | Female Median (IQR) | $p$ Value |
|---|---|---|---|---|
| Energy (kcal/day) | 2528 (1004) | 2787 (1064) | 2352 (902) | <0.001 |
| Carbohydrates (%E/day) | 64.6 (7.9) | 64.0 (8.0) | 64.9 (8.0) | 0.005 |
| Weighted GI | 63.1 (3.9) | 63.0 (3.7) | 63.2 (3.9) | 0.083 |
| Glycemic load (GL/day) | 234.7 (48.3) | 235.4 (50.3) | 234.6 (48.4) | 0.205 |
| Total dietary fiber (g/day) | 30.0 (7.9) | 29.7 (8.4) | 30.0 (7.7) | 0.759 |
| Protein (%E/day) | 11.2 (1.5) | 11.3 (1.5) | 11.1 (1.5) | 0.361 |
| Total fat (%E/day) | 23.5 (6.2) | 23.4 (6.1) | 23.5 (6.3) | 0.610 |
| Total saturated fatty acid—SFA (%E/day) | 8.6 (3.0) | 8.6 (3.2) | 8.7 (3.0) | 0.280 |
| Total Poly unsaturated fatty acid—PUFA (%E/day) | 6.5 (3.6) | 6.6 (3.5) | 6.3 (3.8) | 0.288 |
| Total mono unsaturated fatty acid—MUFA (%E/day) | 6.9 (2.1) | 6.9 (2.1) | 6.9 (2.1) | 0.649 |
| Trans fatty acid—TFA (%E/day) | 0.03 (0.07) | 0.04 (0.07) | 0.03 (0.06) | 0.011 |
| Cereals refined (g/day) | 342.0 (107.6) | 343.4 (112.8) | 340.7 (105.7) | 0.288 |
| Pulses and legumes (g/day) | 52.6 (0.2) | 52.6 (0.2) | 52.6 (0.2) | 0.195 |
| Dairy products (g/day[†††]) | 372.3 (279.1) | 359.9 (291.1) | 377.6 (272.8) | 0.228 |
| Tubers (g/day) | 24.9 (19.9) | 26.2 (22.4) | 24.1 (19.1) | 0.072 |
| Fruits and vegetables (g/day[¶¶]) | 337.8 (149.2) | 331.0 (145.2) | 342.0 (147.4) | 0.061 |
| Meat and poultry (g/day) | 18.8 (18.0) | 19.5 (21.5) | 18.4 (15.1) | 0.202 |
| Fish and sea foods (g/day) | 17.2 (17.3) | 17.0 (19.8) | 17.3 (15.5) | 0.178 |
| Nuts and oil seeds (g/day) | 20.6 (10.8) | 20.1 (12.3) | 21.0 (9.7) | 0.266 |
| Visible fat and oil (g/day) | 33.1 (11.7) | 32.8 (12.0) | 33.2 (11.5) | 0.292 |
| Added sugar (g/day) | 13.3 (16.9) | 12.6 (19.6) | 13.7 (15.1) | 0.281 |
| Added salt (g/day) | 8.5 (3.0) | 8.6 (3.4) | 8.5 (2.8) | 0.682 |
| Sunflower oil[*] | 914 (66.4) | 389 (42.6) | 525 (57.4) | 0.126 |
| Palmolein oil[*] | 335 (24.3) | 124 (37.0) | 211 (63.0) | |
| Groundnut oil[*] | 89 (6.5) | 39 (43.8) | 50 (56.2) | |
| Peanut oil[*] | 37 (2.7) | 20 (3.5%) | 17 (45.9) | |

Median inter quartile range (IQR) in parentheses and statistical test was done by Mann–Whitney $U$ test for such variables ($p < 0.01$). Chi-square used for categorical variable. Energy adjusted by residual method [15].

[¶¶] Fruits and vegetables include fruits, leafy vegetables, other vegetables and roots.

[†††] Dairy products include milk, yoghurt and buttermilk.

[*] $n$ (%).

**Table 3 – Multivariate Poisson regression model and partial population attributable risk for type 2 diabetes.**

| [*]Multivariate Poisson regression model Risk factors[*] | Overall Adjusted RR (95%CI) | Male Adjusted RR (95%CI) | Female Adjusted RR (95%CI) |
|---|---|---|---|
| Age (continuous variable) | 1.04 (1.03–1.04)[^] | 1.04 (1.03–1.06)[^] | 1.03 (1.02–1.04)[^] |
| Gender (male) | 1.48 (1.17–1.86)[^] | – | – |
| Family history of diabetes (positive) | 2.63 (2.10–3.30)[^] | 6.37 (4.41–9.20)[^] | 1.42 (1.04–1.94)[^] |
| Abdominal obesity (waist circumference: males ≥90 cm; females ≥80 cm) | 1.63 (1.21–2.20)[^] | 1.43 (0.96–2.13) | 1.73 (1.15–2.61)[^] |
| Generalized obesity (BMI > 23 kg/m$^2$) | 1.51 (1.13–2.03)[^] | 2.13 (1.37–3.30)[^] | 1.34 (0.92–1.94) |
| Hypertriglyceridemia (≥150 mg/dl) | 1.49 (1.18–1.88)[^] | 1.27 (0.90–1.80) | 1.49 (1.08–2.05)[^] |
| Low HDL (males <40 mg/dl; females <50 mg/dl) | 1.37 (1.07–1.75)[^] | 1.38 (0.98–1.94) | 1.48 (1.05–2.10)[^] |
| Physical inactivity (<600 MET min/week) | 1.58 (1.23–2.03)[^] | 1.55 (1.08–2.21)[^] | 1.53 (1.05–2.21)[^] |
| Household income [<5000[#] INR/Month (USD <83/month)] | 1.92 (1.48–2.48)[^] | 2.44 (1.65–3.60)[^] | 1.98 (1.39–2.83)[^] |
| **Partial population attributable risk (PAR$_p$)[$]** | **PAR$_p$% (95% CI)** | **PAR$_p$% (95% CI)** | **PAR$_p$% (95% CI)** |
| Generalized obesity (≥23 kg/m$^2$) | 37.4 (32.6, 41.9) | 52.6 (52.4, 52.8) | 29.1 (15.5, 41.6) |
| Abdominal obesity (waist circumference ≥90 cm male≥80 cm female) | 41.1 (28.1, 52.6) | 40.1 (18.3, 58.1) | 44.4 (21.6, 62.6) |
| Low HDL (males <40 mg/dl; females <50 mg/dl) | 27.4 (20.5, 34.0) | 29.2 (22.2, 35.9) | 30.9 (14.3, 45.7) |
| Hypertriglyceridemia (≥150 mg/dl) | 15.5 (4.8, 25.9) | 19.7 (10.8, 28.3) | 10.7 (−4.5, 25.4) |
| Diet Score (>50th percentile)[#] | 30.1 (16.0, 43.0) | 29.8 (−2.0, 56.1) | 42.6 (10.7, 66.6) |
| Physical inactivity (<600 MET min/week) | 32.8 (26.6, 38.7) | 38.3 (29.8, 46.1) | 27.8 (15.1, 39.5) |
| **Risk factors combination 1[¥]** = Diet score > 50th percentile + physical inactivity (<600 MET min/week) | 51.7 (35.8, 64.7) | 54.0 (23.3, 74.9) | 59.3 (25.6, 80.2) |
| **Risk factors combination 2[¥]** = risk factors combination 1 + generalized obesity BMI (≥23 kg/m$^2$) | 62.7 (39.4, 78.5) | 76.0 (54.6, 88.1) | 72.1 (36.1, 89.4) |
| **Risk factors combination 3[¥]** = risk factors combination 1 + abdominal obesity (waist circumference ≥90 cm male ≥80 cm female) | 70.8 (52.7, 82.7) | 70.5 (36.2, 88.0) | 79.2 (43.3, 93.4) |
| **Risk factors combination 4[¥]** = risk factors combination 3 + BMI (≥23 kg/m$^2$) | 73.2 (46.0, 87.8) | 78.2 (48.6, 91.7) | 82.2 (37.6, 95.9) |
| **Risk factors combination 5[¥]** = risk factors combination 4 + hypertriglyceridemia (≥150 mg/dl) | 75.4 (46.5, 89.8) | 79.6 (50.2, 92.5) | 84.7 (37.5, 97.0) |
| **Risk factors combination 6[¥]** = risk factors combination 5 + low HDL (males <40 mg/dl; females <50 mg/dl) | 80.7 (53.8, 92.7) | 84.3 (55.8, 95.0) | 86.3 (32.1, 97.9) |

[*] Variables with a $p$ value <0.2 in univariate analysis were entered into the multivariate Poisson regression model.
[^] $p$ Value <0.05 significant.
[$] Adjusted for non modifiable risk factors such as: age (yrs), family history of diabetes (yes/no), household income (income/month < Rs. 5000 [USD < 83], >Rs. 5000 [USD > 83]) and gender.
[#] Diet risk score: developed based on 3 food groups (energy adjusted refined cereal, fruit and vegetable, and dairy products) and 1 nutrient—(MUFA (g/d)). Participants were assigned quartile scores of all dietary factors which were then summed and the total score was further categorized into quartiles with ≤ the 50th percentile of the diet score as the reference.
[¥] The diet score was adjusted for non modifiable risk factors + abdominal obesity (waist circumference ≥90 cm [men] and ≥80 cm [women]), physical inactivity (<600 MET/week), energy adjusted dietary fiber (quartiles g/day), energy adjusted meat and poultry (quartiles g/day), energy adjusted protein (quartiles g/day), energy adjusted added sugar (quartiles g/day) poly unsaturated fatty acid (quartiles g/day).

[PAR$_p$: 32.8% (26.6–38.7)]. The PAR$_p$ for the diet score was 30.1% 16.0–43.0. In combination, the diet score and physical inactivity contributed 51.7%(95%CI: 35.8–64.7)of the PAR$_p$ for diabetes, three risk factors (diet + physical inactivity + obesity both (generalized and abdominal obesity) 73.2% (46.0–87.8), 4 risk factors (diet + physical inactivity + obesity + hypertriglyceridemia), 75.4% (46.5–89.8) and 5 risk factors (diet + physical inactivity + generalized obesity + abdominal obesity + hyper triglyceridemia + low HDL), 80.7% (53.8–92.7) of the PAR$_p$ for diabetes mellitus.

Fig. 2 shows the relative risk for diabetes by quartiles of intake of various dietary factors after adjusting for age, gender, family history of diabetes, physical inactivity, generalized obesity, abdominal obesity, household income, total energy, energy adjusted saturated fatty acid (SFA g/day in quartiles), and dietary fiber (g/day in quartiles) for the selected diet variables. In addition, added sugars (g/d) and meat intake (g/d) were further adjusted for dairy intake. The risk for diabetes increased with increasing quartiles of refined cereal intake (Highest quartile RR 1.85[95%CI: 1.20–2.87]), with decreasing quartiles of fruit and vegetable intake (Highest quartile RR 0.66 [0.44–0.99]), dairy (Highest quartile RR 0.44 [0.28–0.68]) and MUFA (Highest quartile RR 0.65 [0.41–1.03]), and with increasing quartiles of the diet risk score (Highest quartile RR 2.14 [1.26–3.63]). Fig. 2 also shows that the risk for diabetes increases with increasing quartiles of time spent viewing TV (Highest quartile RR 1.84 [1.36–2.49]) and sitting (Highest quartile RR 2.09 [1.42–3.05]).

## 4. Discussion

The present paper reports, for the first time, the relative contributions of various modifiable risk factors, singly and in

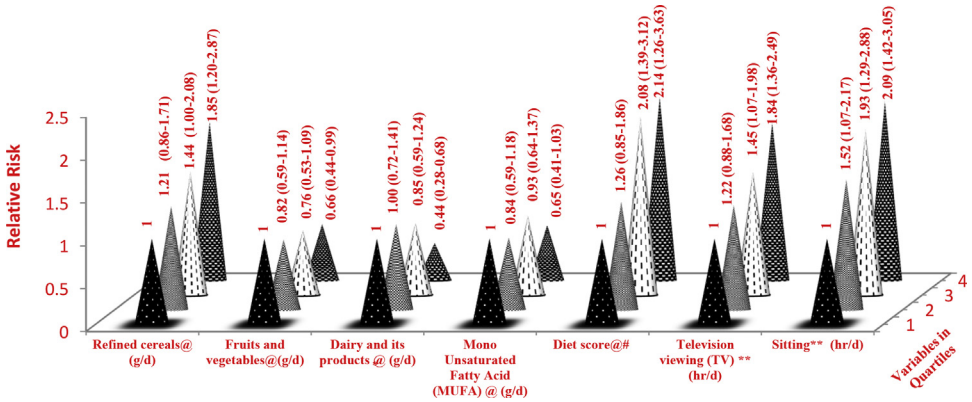


**Fig. 2 – Distribution of modifiable risk factors and relative risk for type 2 diabetes.**

combination, to the incidence of diabetes in an Asian Indian population. Our results show that more than 80% of incident diabetes cases could be prevented by modifying five easily identifiable risk factors: obesity, physical inactivity, diet, hypertriglyceridemia and low HDL cholesterol. A total of 51.7% could be prevented if only diet and physical activity were improved and this further increases to 70.8% if abdominal obesity were to be controlled as well.

Obesity has long been recognized as a strong risk factor for type 2 diabetes (T2DM). In a pooled dataset from Finland and a multiethnic population of Hawaii [4,18], generalized obesity emerged as the strongest contributor to incident diabetes. Similarly, excess weight contributed significantly to diabetes among Tehranian (Iranian) women (but less so in men) [6]. Overweight and obesity contributed 23.3 and 37.1% respectively to the adjusted PAR for diabetes among Tehranian adults, a figure comparable to the 37.4% reported for generalized obesity in our study. However, abdominal obesity appears to contribute more to the $PAR_p$ for diabetes than generalized obesity, in our population. This is probably a reflection of the ''Asian Indian phenotype'', which is characterized by high levels of visceral fat at lower levels of BMI [19]. However, generalized obesity contributed more to the $PAR_p$ for diabetes among males while abdominal obesity contributed more among females. An earlier study from this population has also shown that abdominal obesity better predicts obesity-related metabolic risk for women, while generalized obesity is a better predictor in men [20]. Steps to combat obesity in our population should therefore focus on reducing abdominal obesity as well as generalized obesity.

Numerous studies have shown the association between sedentary behavior, TV viewing and diabetes [21–23], but few have looked at their relative contribution to the PAR for diabetes. A systematic review of three cohort studies found that physical inactivity contributed 3% to 29% to the PAR for diabetes [24], while Bull showed that PAR for physical inactivity ranged from 5% in Canada to 13% in Finland [25]. Our results show that physical inactivity independently contributes a considerably higher proportion (32.8%) to the diabetes burden, probably reflecting the high prevalence of this risk factor in India [26]. Our results show that individuals who spend less than 3 h sitting and 1 h watching television per day had the least risk of diabetes; however, the risks associated with these sedentary behaviors exist along a continuum and reduction of any magnitude in the time spent in these sedentary pursuits is likely to be beneficial.

Our results suggest that a low risk diet score, characterized by refined cereal intake below 300 g/day and approximate daily intake of 400 g fruit and vegetables, 500 g dairy and 20 g (median 7.9%E/day) MUFA (derived from edible oil and nuts in this population)could prevent 30% of cases of diabetes. While the use of quantiles of intake in our risk score limits the appropriateness of comparisons, our results suggest that processed meat, trans-fats and low PUFA/saturated fat ratio which contribute to the risk of diabetes in other populations [3,5] seem to be less important in the Indian population, probably on account of low levels of consumption.

Earlier studies in white Caucasians, such as the Nurses' Health Study [3], the Cardiovascular Health Study [5], and a pooled sample of two Finnish cohorts [4] have shown that the major proportion of incident cases of diabetes could be attributed to obesity, physical inactivity, poor diet, smoking and alcohol use. While our results reiterate the pivotal role of physical inactivity and diet in the development of diabetes, it is important to note that our definition of a poor diet score differed significantly from those used in the studies quoted above. Also, neither alcohol intake nor smoking contributed significantly to the $PAR_p$ for diabetes in our population, likely due to the low prevalence of social alcohol intake in the population and the virtual absence of smoking and alcohol use among women.

While obesity, hypertriglyceridemia and low HDL cholesterol can be easily identified in the population, the extent to which they could be favorably modified by lifestyle interventions remains a matter of conjecture. Our results, however, show that improvement in physical activity levels and dietary profile could, by themselves, prevent more than 50% of cases of incident diabetes; these efforts may, in addition, have salutary effects on the levels of obesity, hypertriglyceridemia and HDL cholesterol. The combination of PARs contributed by individual risk factors adding up to more than 100% suggests the overlapping of risk factors and interactions among them as reported by earlier studies [3,27].

This paper represents the first assessment of $PAR_p$ for diabetes in an Asian Indian population. While earlier studies have attempted to quantify the risk for diabetes conferred by various risk factors, alone or in combination, in white

Caucasian populations [3], they have limited applicability to Asian Indians on account of differences in the population prevalence of these risk factors between various ethnic groups. This is particularly so with regard to dietary risk factors, since dietary patterns vary widely between populations. For instance, the adverse dietary pattern associated with diabetes in Caucasian populations consisted of high intake of processed meat, trans-fat and sweetened beverages, whereas in our population, intake of refined cereals was an important component of the unhealthy diet pattern [28], contributing to the $PAR_p$ for diabetes. These results are probably a reflection of the low levels of consumption of processed meat and sweetened beverages, and high levels of refined cereal intake in the Asian Indian population; nonetheless, this information is of paramount importance if meaningful recommendations are to be made for preventing diabetes in this region.

Our study has certain limitations. First, the population studied was from an urban area in India, thereby limiting the generalisablity of our findings to the rural areas. Second, the use of interviewer administered questionnaires for assessing physical activity and diet could have introduced an element of measurement error/bias, but since it is not related to outcome assessment this would likely attenuate our estimates to the null. Third, there was no year-by-year follow-up data and we relied on self-report for diagnosis of diabetes in the interim. However, each such case was checked against available medical records to ensure accuracy of the diagnosis.

The strengths of the study lie in its prospective design and high follow-up response rates. Moreover, our results provide a clear and simple public health message by identifying, for the first time, the relative contributions of several easily identifiable and potentially modifiable risk factors to the development of diabetes in the Asian Indian population.

>In conclusion, our results show that more than 80% of cases of diabetes can be prevented in this Asian Indian population by modifying five risk factors. This information is likely to be of considerable use in planning, implementing and evaluating effective strategies for the prevention of diabetes in this region. However, efforts to popularize a healthy diet pattern will have to contend with formidable barriers such as easy availability of cheap refined grains through government-subsidized foods (i.e., India's Public Distribution System) and prohibitive costs of fruit and vegetables as well as healthy oils; and those intended to increase the levels of physical activity will need to address concerns such as lack of safe and accessible locations to exercise. Concerted action is required at the individual, societal and governmental levels to overcome these barriers, thereby enabling adoption of healthier lifestyles in the Asian Indian population.

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Nil.

## Conflict of interest statement

The authors declare that they have no conflict of interest.

## Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

## Author contributions

RMA, RU and VM were involved in conception and design of this study, helped in the interpretation of data and revised all drafts of the article. CSS, MD and RP were involved in acquisition, analysis and interpretation of data. VS, DHN, SS and NL helped in the analysis and interpretation of data. VaM, VSB, SAP and FBH provided inputs for statistical analysis and interpretation of the data. VM 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. RMA wrote the first draft of the manuscript and all the other authors were involved in revising it critically for important intellectual content. All authors approved the final version of the manuscript.

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