DOI: 10.1111/dme.13071

Short Report: Epidemiology

Impact of lifestyle intervention in primary prevention of Type 2 diabetes did not differ by baseline age and BMI among Asian-Indian people with impaired glucose tolerance

A. Nanditha[1,2], C. Snehalatha[1,2], J. Ram[1], S. Selvam[1], L.Vijaya[1], S. A. Shetty[1,2], R. Arun[1,2] and A. Ramachandran[1,2]

[1]India Diabetes Research Foundation and [2]Dr. A. Ramachandran's Diabetes Hospitals, Chennai, India

Accepted 11 January 2016

Abstract

Aim To investigate whether the effectiveness of lifestyle interventions on the incidence of diabetes was influenced by the baseline age and BMI of the Asian-Indian participants with prediabetes.

Methods Pooled data, obtained from two of our Indian Diabetes Prevention Programmes (2006, n=236 and 2013, n=473; total N=709) which had similar baseline characteristics and intervention principles, were analysed. For the present secondary analysis we dichotomously categorized the participants' baseline age (<45 and ≥45 years) and BMI (<25.0 and ≥ 25.0 kg/m^2). Glycaemic status was ascertained at 6-monthly intervals by oral glucose tolerance tests. The incidence rates of diabetes and relative risk reduction in both the intervention and the control group were calculated for categories of baseline age and BMI. Interactions between the intervention and baseline age and BMI on diabetes risk were also analysed.

Results Incident diabetes was diagnosed in 227 of the total 709 participants (32.0%) [control group 139 participants (38.8%) vs intervention group 88 participants (24.2%)] during the median follow-up period of 2 years. The overall relative risk reduction was 35.4% (95% CI 19.3–48.3). Lifestyle intervention was equally effective in both age groups [relative risk reduction in those aged <45 years: 43.7% (95% CI 19.8–60.5) and in those aged ≥ 45 years: 28.9% (95% CI 5.3–46.6) P for interaction = 0.52] and in categories of BMI [BMI <25 kg/m^2: 36.1% (95% CI 9.5–54.9); and BMI ≥ 25 kg/m^2: 34.8% (95% CI 12.9–51.2); P for interaction = 0.95].

Conclusions In Asian-Indian individuals with prediabetes, the effectiveness of lifestyle intervention was not modified by baseline age and BMI.

Diabet. Med. 00, 000–000 (2016)

Introduction

Systematic diabetes prevention studies have unequivocally shown that Type 2 diabetes can be prevented and/or delayed in people with prediabetes by sustained improvements in lifestyle modification [1]. In the Finnish Diabetes Prevention Study (DPS) [2] and the Diabetes Prevention Program (DPP) in the USA [3] the reduction in incidence of diabetes was mainly attributed to the benefits of weight reduction among people with impaired glucose tolerance (IGT); however, in the Asian diabetes prevention studies, such as the Indian Diabetes Prevention Programme 1 (IDPP-1) [4] and the Chinese Da Qing study [5], the reduction in incidence of diabetes after lifestyle intervention was independent of baseline BMI or weight reduction during follow-up. The DPP study showed that lifestyle intervention was equally effective for prevention of diabetes when the analysis was stratified by baseline BMI [relative risk reductions: BMI 22.0 to <30 kg/m^2, 65% (95% CI 46–77); BMI 30 to < 35 kg/m^2, 61% (95% CI 40–75); and BMI ≥ 35.0 kg/m^2, 51% (95% CI 34–63)] compared with placebo [3]. Sub-analysis of the Da Qing study also showed that lifestyle intervention was equally effective when the participants were stratified by baseline BMI (<25.0 kg/m^2 vs ≥25.0 kg/m^2) [5]. The influence of baseline BMI on the effect of lifestyle interventions has not been ascertained in an Asian-Indian population.

Correspondence to: A. Ramachandran. E-mail: ramachandran@vsnl.com

What's new?

- In Western diabetes primary prevention programmes the effectiveness of lifestyle intervention has been shown to be influenced by baseline BMI and age.
- The present study assessed the effectiveness of lifestyle intervention on the incidence of diabetes among Asian-Indian people with impaired glucose tolerance, stratified by age and BMI.
- The results showed that the impact of lifestyle intervention was similar among non-obese and obese Asian-Indians with impaired glucose tolerance in different age categories

The aim of the present study, therefore, was to assess whether baseline BMI and age influences the effectiveness of lifestyle interventions on the incidence of diabetes using pooled data from two Indian Diabetes Prevention Programmes [4,6].

Participants and methods

Pooled data from two primary prevention programmes, the IDPP-1 study [4] and another study completed in 2013 [6], were included for the present analysis. The IDPP-1 (2006) study was a 3-year, prospective randomized controlled trial in Asian-Indian people with persistent IGT on two repeated oral glucose tolerance tests (OGTTs) [4]. The primary cohort comprised 531 (421 male, 110 female) participants who were divided into four study groups: group 1, who received standard advice (control group, n=136); group 2, who received moderate intensive lifestyle advice regularly for 3 years (n=133); group 3, who were treated with metformin 500 mg/day (n=133); and group 4, who were treated with both lifestyle intervention and metformin 500 mg/day (n=129). The study showed that both lifestyle intervention and metformin were equally effective (relative risk reductions of 28.5% and 26.4%, respectively) in the prevention of diabetes in this cohort. There was no additive effect when metformin was added to lifestyle intervention (relative risk reduction -28.2%). For the present analysis, groups 1 and 2 were included.

In the second primary prevention study (2013) [6], a total of 537 men were randomized into two groups: a control group, who received standard lifestyle advice only at baseline and an intervention group, who, in addition to the standard care advice, also received tailored text messages on healthy lifestyle habits over the period of 2 years. A total of 517 participants completed the 2-year follow-up. The study showed for the first time that reminders about healthy lifestyle through text messaging is an effective and acceptable tool with which to deliver and support lifestyle modification to prevent Type 2 diabetes in Asian-Indian men with IGT (relative risk reduction 36.0%) [6].

Participants from the two studies were combined for the present analysis because all of them had persistent IGT on two OGTTs. Baseline BMI (2006 study: 26.0 ± 3.5 kg/m^2; 2013 study: 25.8 ± 3.2 kg/m^2; P=0.432) and age (2006 study: 45.7 ± 5.6 years; 2013 study: 46.1 ± 4.7 years; P=0.256) were similar in the two studies. At annual visits, all participants underwent an OGTT. During the 6-monthly interim visits; i.e. at 6, 18 and 30 months, a 2-h post-glucose-load test was performed. If the blood glucose result was ≥11.1 mmol/l, a confirmatory OGTT was performed within 1 week using venous plasma sampling in the fasting state, at 30 min and at 2 h after 75-g glucose ingestion.

The primary outcome was development of diabetes as classified by the WHO recommendations [7]; a fasting plasma glucose ≥7.0 mmol/l and /or a 2-h post-glucose-load value ≥11.1 mmol/l during an OGTT.

Plasma glucose was measured using the glucokinase method in the IDPP-1 study and the hexokinase method in the 2013 study. Plasma insulin was measured using a radioimmuno assay kit (Diasorin, Saluggia, Italy; sensitivity of <24 pmol/l and intra- and interassay coefficients of variation <10%) in the IDPP-1 study and by electrochemiluminiscence assay (Elesys Cobas e411 auto-analyzer; Roche diagnostics, Mannheim, Germany; coefficient of variation <3%; detection range: 1.39–6945 pmol/l) in the 2013 study. Results obtained using the two assays were strongly correlated. Insulin resistance [8] was calculated using the formula: homeostatic model assessment of insulin resistance (HOMA-IR): (fasting insulin * fasting glucose)/22.5. The oral disposition index (total AUC glucose/insulin) * Matsuda's insulin sensitivity index was used as a measure of β-cell function [9].

For the present analyses we selected 709 participants (236/269 from the IDPP-1 study and 473/517 from the 2013 study) who had baseline and follow-up data on anthropometry, glycaemic outcomes, HOMA-IR and β-cell function.

Statistical analysis

Age categories (<45 and ≥45 years) using the midpoint of the age at recruitment (35–55 years) and BMI categories (<25.0 and ≥ 25.0 kg/m^2) based on the criteria used for obesity in Asian people [10] were used in the analyses.

Continuous variables were expressed as mean ± SD values and evaluated using Student's t-test for normally distributed variables. For skewed variables, values were expressed as medians (interquartile range) and analysed using the Mann–Whitney test. The chi-squared statistic test was applied for categorical variables. Absolute risk reduction, also known as the risk difference, was calculated as the difference between the control event rate and experimental event rate. The 95% CI of the absolute risk reduction was calculated using the formula: absolute risk reduction ±1.96 × sqrt [control event rate × (1 - control event rate)/ no. of control participants + experimental event rate × (1 - experimental event rate)/ no. of experimental patients]. Relative risk reduction was computed using the formula: |experimental event rate - control event rate|/control event rate [11]. The heterogeneity of treatment effect between the two estimates were calculated using the standard methods [12,13]. Significant heterogeneity indicates that the effect of intervention differed according to the values of the covariates. All analyses were performed using IBM SPSS 19.0 software (IBM Corp., Armonk, NY, USA).

Results

The baseline characteristics of the study participants grouped according to age and BMI are shown in Table 1. There were 358 and 351 participants in the control and intervention groups, respectively. There was a greater proportion of overweight/obese than non-obese participants [410 (57.8%) had a BMI ≥ 25 kg/m^2 vs 299 (42.2%) with a BMI < 25 kg/m^2] owing to the selection of a high-risk group.

Fasting plasma glucose levels were higher (P=0.004) and the oral disposition index was lower (P=0.005) among the older age group. As expected, body weight and HOMA-IR values were higher in the obese than in the non-obese group (P<0.0001).

At the end of the follow-up period, among 709 participants, incident diabetes was diagnosed in 227 participants (32.0%): 139 (38.8%) in the control group and 88 (24.2%) in the intervention group. The median (interquartile range) cumulative relative risk reduction was 35.4% (19.3–48.3%) and the absolute risk reduction was 13.8% (6.9–20.4%).

The effects of the lifestyle intervention among subgroups of age and BMI on the incidence of diabetes are shown in Table 2. Lifestyle intervention was effective in both age groups [relative risk reduction <45 years: 43.7% (95% CI 19.8–60.5); ≥ 45 years: 28.9% (95% CI 5.3–46.6); P for interaction = 0.52] and in both the non-obese [BMI < 25 kg/m^2: 36.1 (95% CI 9.5–54.9)] and the obese [BMI ≥ 25 kg/m^2: 34.8% (95% CI 12.9–51.2); P for interaction = 0.95] categories. There was no evidence of heterogeneity of treatment effects when the participants were stratified based on age and BMI .

Discussion

The main observations of the present analysis in Asian-Indian people with IGT were that the effectiveness of moderate lifestyle modification was not altered based on baseline age and BMI. Despite the presence of significantly higher insulin resistance in the obese group and lower β-cell response in the older age group, the effectiveness of lifestyle modification was similar among the age and BMI categories. Contrary to our findings, *post hoc* analysis of the Finnish DPS [14] and the DPP [15] showed that the lifestyle intervention was most effective among the older (≥61 years) age group than in the younger group. Similarly to the present study, however, it was noted in the Finnish DPS that the effect of lifestyle intervention was of the same magnitude regardless of baseline BMI (P for interaction = 0.750) [14]. The subgroup analysis of the DPP showed that lower baseline body weight (~10 kg) was associated with a reduced risk of developing diabetes in the intensive lifestyle intervention group [hazard ratio 0.88 (95% CI 0.81–0.96)] [15]. It should be noted that the participants in the present study had a much lower baseline BMI and age compared with participants in the DPP and the DPS, therefore, a comparison with the above findings may not be appropriate.

The relationship between obesity and diabetes prevalence is complex and appears to be modified by ethnicity [16]. India, for instance, has a much lower prevalence of obesity (BMI ≥ 30

Table 1 Baseline characteristics of the participants grouped according to age and BMI (n=709)

Variables	Age < 45 years (n=299)	Age ≥ 45 years (n = 410)	P
Height, cm	165.9 ± 7.5	165.4 ± 6.9	0.360
Weight, kg	71.8 ± 10.1	70.4 ± 10.2	0.067
BMI, kg/m^2	26.1 ± 3.1	25.7 ± 3.5	0.178
Fasting plasma glucose, mmol/l	5.5 ± 0.7	5.6 ± 0.6	0.004
2-h plasma glucose, mmol/l	8.7 ± 0.8	8.7± 0.8	0.796
HOMA-IR	3.3 (2.3–4.7)	3.4 (2.3–4.7)	0.669
Disposition index	154.5 (117.5–193.6)	140.6 (109.3–176.4)	0.004
Variables	**BMI < 25 kg/m^2 (n=299)**	**BMI > 25 kg/m^2 (n = 410)**	**P**
Age, years	46.3 ± 4.9	45.8 ± 5.1	0.220
Height, cm	166.7 ± 6.9	164.9 ± 7.3	0.001
Weight, kg	64.2 ± 6.5	75.9 ± 9.6	<0.0001
Fasting plasma glucose, mmol/l	5.5 ± 0.6	5.6 ± 0.6	0.403
2-h plasma glucose, mmol/l	8.7 ± 0.81	8.8± 0.8	0.254
HOMA-IR	2.9 (2.1–4.2)	3.7 (2.7–5.2)	<0.0001
Disposition index	149.6 (112.9–187.2)	144.5 (113.8–184.1)	0.845

HOMA-IR, homeostatic model assessment of insulin resistance.
Values are mean ± SD or median (interquartile range).

Table 2 Effects of the lifestyle intervention among subgroups of age and BMI on the incidence of diabetes (n=709)

	Number			Incidence of diabetes				*P* for interaction		
	Total	Control	Intervention	Control	Intervention	Absolute risk reduction (95% CI), %	Relative risk reduction (95% CI), %	Ratio of relative risk (95% CI)	Z score	*P*
Over all	709	358	351	139 (38.8)	88 (25.1)	13.8 (6.9–20.4)	35.4 (19.3–48.3)	–	–	–
Age										
<45 years	299	149	150	60 (40.2)	34 (22.7)	17.6 (7.1–27.6)	43.7 (19.8-60.5)	1.52 (0.4–5.3)	0.65	0.52
≥ 45 years	410	209	201	79 (37.8)	54 (26.9)	10.9 (1.9–19.7)	28.9 (5.3–46.6)			
BMI										
<25.0 kg/m^2	299	152	147	56 (38.1)	37 (24.3)	13.8 (3.3–23.9)	36.1 (9.5–54.9)	1.05 (0.3–3.2)	0.06	0.95
≥ 25.0 kg/m^2	410	199	211	83 (39.3)	51 (25.6)	13.7 (4.6–22.4)	34.8 (12.9–51.2)			

Relative risk was calculated for each stratum. Calculations were for comparisons between two estimated relative risks.

kg/m^2) than the USA but higher rates of Type 2 diabetes [17]. In addition, the risk of diabetes in Asian populations increases at a relatively lower BMI threshold than in European populations [18,19]. The recently published UK biobank study showed that, compared with white people with a BMI of ≥ 30 kg/m^2, South-Asian people had an equivalent prevalence of diabetes at a BMI ≥ 22.0 kg/m^2 in women and 21.6 kg/m^2 in men, values which were at the lower end of the normal BMI range for white populations [20]. A meta-analysis of 22 studies in healthy individuals of European origin showed that average weight change with lifestyle intervention differed only to a small extent among people with a BMI between 25 and 40 kg/m^2 [21]. This implied that the intervention was equally effective for different BMI groups.

The present analysis was not powered to assess the significance of effects within the subgroups, nor was this test prespecified. The participants enrolled in these primary prevention programmes had narrow age and BMI ranges and therefore the effectiveness of the lifestyle intervention in broader categories (for instance, age >60 years and/or BMI <23.0 kg/m^2) need to be studied. Another limitation is that a sensitivity analysis with a lower BMI threshold of <23 kg/m^2 could not be carried out, as the number of participants in that category was small compared with the other two categories (23–25 kg/m^2 and ≥ 25 kg/m^2). Asian Indians develop Type 2 diabetes at a much younger age and lower BMI than white people [18,19].

The present analysis showed that lifestyle intervention was equally effective among non-obese and obese individuals and also in both the lower (<45 years) and higher (≥ 45 years) age categories.

Funding sources

The 2013 prevention study was funded by the UK India Education and Research Initiative (grant number IND/CONT/06-07/187E) and partly funded by the World Diabetes Foundation (WDF 08- 406).

Competing interests

None declared.

Acknowledgements

We gratefully acknowledge Mary Simon and C.K. Sathishkumar for their help in carrying out the studies.

References

1 Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT *et al*. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* 2007; **334**: 299.

2 Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P *et al*. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; **344**: 1343–1350.

3 Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA *et al*. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; **346**: 393–403.

4 Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006; **49**: 289–297.

5 Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX *et al*. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997; **20**: 537–544.

6 Ramachandran A, Snehalatha C, Ram J, Selvam S, Mary S, Nanditha A *et al*. Effectiveness of mobile phone messaging in prevention of type 2 diabetes by lifestyle modification in men in India: a prospective, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol* 2013; **1**: 191–198.

7 Report of the Expert Committee on the Diagnosis, Classification of Diabetes Mellitus. *Diabetes Care* 1997; **20**: 1183–1197.
8 Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412–419.
9 Ram J, Snehalatha C, Selvam S, Nanditha A, Shetty A, Godsland I *et al*. The oral disposition index is a strong predictor of incident diabetes in Asian Indian prediabetic men. *Acta Diabetologica* 2015: 1–9.
10 Report of the WHO consultation, "Obesity preventing and managing the global epidemic" World Health Organization – Technical Report Series. No. 891. Geneva: WHO, 2000; 1–253.
11 Irwig L, Irwig J, Trevena L, Sweet M. Smart Health Choices: Making Sense of Health Advice. Chapter 18, Relative risk, relative and absolute risk reduction, number needed to treat and confidence intervals. London: Hammersmith Press, 2008. Available at http://www.ncbi.nlm.nih.gov/books/NBK63647/.
12 Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ* 2003; **326**: 219.
13 Altman DG, Matthews JN. Statistics notes. Interaction 1: Heterogeneity of effects. *BMJ* 1996; **313**: 486.
14 Lindstrom J, Peltonen M, Eriksson JG, Aunola S, Hamalainen H, Ilanne-Parikka P *et al*. Determinants for the effectiveness of lifestyle intervention in the Finnish Diabetes Prevention Study. *Diabetes Care* 2008; **31**: 857–862.
15 Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L *et al*. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care* 2006; **29**: 2102–2107.
16 Raji A, Seely EW, Arky RA, Simonson DC. Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. *J Clin Endocrinol Metab* 2001; **86**: 5366–5371.
17 Ramachandran A, Snehalatha C, Samith A, Shetty SA, Arun N, Susairaj P. Obesity in Asia–is it different from the rest of the world. *Diabetes Metab Res Rev* 2012; **28**: 47–51.
18 Ramachandran A, Snehalatha C, Vijay V. Low risk threshold for acquired diabetogenic factors in Asian Indians. *Diabetes Res Clin Pract* 2004; **65**: 189–195.
19 The DECODE-DECODA study Group. Age, body mass index and type 2 diabetes-associations modified by ethnicity. *Diabetologia* 2003; **46**: 1063–1070.
20 Ntuk UE, Gill JM, Mackay DF, Sattar N, Pell JP. Ethnic-Specific Obesity Cutoffs for Diabetes Risk: Cross-sectional Study of 490,288 UK Biobank Participants. *Diabetes Care* 2014; **37**: 2500–2507.
21 Barte JC, Veldwijk J, Teixeira PJ, Sacks FM, Bemelmans WJ. Differences in weight loss across different BMI classes: a meta-analysis of the effects of interventions with diet and exercise. *Int J Behav Med* 2014; **21**: 784–793.

