Original article

Weight status of the first-degree relatives of patients with type 2 diabetes based on the glucose tolerance test

Noureddin Soltanian,[1] Ahmad Amini,[1] Bijan Iraj,[2] Gholamreza Askari,[1] Saeed Ebneyamin,[1] Majid Ghias,[1] Hossein Hajian,[1] Arash Zahed,[1] Massoud Amini[3]

[1]Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. [2]Assistant Professor, Department of Internal Medicine, School of Medicine And Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. [3]Professor, Department of Internal Medicine, School of Medicine And Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

Background: This study aimed to compare different body mass index (BMI) categories in individuals with diabetes, prediabetes and normal glucose tolerance among the first degree relatives of type 2 diabetic patients. **Materials and Methods:** A cross-sectional study was conducted during 2005-2007 in Isfahan, Iran. It evaluated 3323 first-degree relatives of diabetic patients selected by consecutive convenient sampling method. Participants were classified as diabetic, prediabetic, and normal glucose tolerance test groups according to the results of 75 g oral glucose tolerance test (OGTT). The analysis of variance (ANOVA) was used for comparison of quantitative variables, and chi square test for comparison of categorical parameters. **Results:** The study population consisted of 3323 individuals including 306 diabetics (98 males and 208 females), 1309 prediabetics (337 males and 972 females), and 1708 normal subjects (430 males and 1278 females). Among diabetic patients, the prevalence of obesity was 48.5% in women and 27.6% in men. Among prediabetics, the corresponding figures were 45.6% and 27.3%, respectively. **Conclusions:** Our findings suggest that men are diagnosed with T2DM at lower BMI than women. Moreover, the alarming high prevalence of overweight and obesity among females necessitates preventing and controlling this underlying problem among females.

Key words: Diabetes Mellitus, Family History, Glucose Tolerance Test, Obesity, Prevention

INTRODUCTION

The role of obesogenic environments, with high-calorie intake and sedentary lifestyle, on the development of obesity and ultimately diabetes is well documented. The causal relationship of obesity and diabetes is strong enough for the term diabesity to be used in experimental and human studies.[1-3] However, genetic background increases this risk of diabetes mellitus.[4-6]

Epidemiological studies have suggested that genetic factors as well as obesity, measured by body mass index (BMI), and abdominal obesity, measured by waist circumference are major risk factors for the development of type 2 diabetes mellitus (T2DM).[7] Positive family history of diabetes can be used as a potential public health tool and an indicator of genetic background.[8,9] It has been demonstrated that having a parent with T2DM increases by two- to four- folds an offspring's risk of developing this disorder.[10-14] However, not all obese individuals are affected by disorders in glucose metabolism and diabetes.[15,16] There are even reports from normal metabolic profile of morbidly obese persons.[17-20]

Middle Eastern countries are expected to have the world's highest increases in the absolute burden of diabetes in the next two decades.[21] National studies have shown high prevalence of obesity,[22] metabolic syndrome,[23] and diabetes in Iran.[24] These high prevalence rates and the aforementioned importance of family history mandate conducting studies in relatives of T2DM patients to determine and to control their risk factors as a high-risk approach for preventing diabetes. This study thus aimed to compare different BMI categories in individuals with diabetes, prediabetes, and normal glucose tolerance among the first degree relatives of T2DM patients.[25]

MATERIALS AND METHODS

This study was a part of the Isfahan Diabetes Prevention Program Study, conducted in 2005-2008 among first degree relatives of T2DM patients.[26] It was carried out by Isfahan Endocrine and Metabolism Research Center (IEMRC) affiliated to Isfahan University of Medical Sciences (IUMS),

Address for correspondence: Ahmad Amini, sfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: amini@med.mui.ac.ir
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Isfahan, Iran. Participants were selected by consecutive convenient sampling from among 3700 individuals aged 35-60 years who were the first degree relatives of T2DM patients. All participants underwent an oral glucose tolerance test after 10-12 hours overnight fasting. Individuals with diabetes, prediabetes, and normal glucose tolerance test, according to the 2005 American Diabetes Association criteria[25] were enrolled in the current study. Those with unknown glucose tolerance state and pregnant women were not recruited.

The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences and the local scientific ethical committee according to the Declaration of Helsinki. All patients gave informed consents prior to the study.

Anthropometric parameters were measured under standard protocol and by using calibrated instruments. Height was measured as the vertical distance from the vertex point to the base of the heels. The reading was recorded to the nearest 0.1 cm. Weight was measured in kilograms by making the subject stand on a weighing machine with minimal clothing without shoes. Weight was recorded with an allowance deducted for clothing. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. A BMI of 18-25 kg/m^2 was considered as normal, 25-29.9 kg/m^2 as overweight, and ≥ 30 kg/m^2 as obese.

Waist circumference was measured at level of maximal point at right iliac crest in mid axillary line in normal respiration.

Blood pressure (BP) was measured twice in a sitting position after 5 minutes resting.

Statistical Analysis:

Statistical analysis was performed by SPSS$_{16.0}$ for Windows (SPSS Inc., Chicago, Illinois, USA). Data is expressed as mean and standard deviation (SD). The analysis of variance (ANOVA) was used for comparison of quantitative variables. Post-hoc and chi-square tests were used for comparison of categorical parameters. P values less than 0.05 were considered as statistically significant.

Results

The study population consisted of 3323 individuals including 306 with diabetes (98 males and 208 females), 1309 with prediabetes (337 males and 972 females), and 1708 with normal glucose tolerance test (430 males and 1278 females). Table 1 presents the demographic, anthropometric and clinical characteristics of all participants. Table 2 shows the results of post hoc tests for continuous variables among participants with diabetes, prediabetes and normal glucose tolerance test. Demographic, anthropometric and clinical characteristics of all participants and the results of post hoc tests for continuous variables among the studied groups based on gender are presented in Tables 3 and 4. In diabetic patients, no significant difference was present between male and female subgroups with regard to age ($p = 0.87$). The subgroups were also identical in mean systolic and diastolic blood pressures ($p = 0.635$ and $p = 0.293$, respectively). However, mean values of weight, BMI, and waist circumference were significantly different between males and females ($p < 0.001$ for all three variables).

Table 1. Demographic, anthropometric and clinical characteristics of diabetic, prediabetic and normal participants

	Age (year)	Sex		Weight (kg)	BMI (kg/m2)	Waist circumference (cm)	Systolic BP (mmHg)	Diastolic BP (mmHg)
		Male	Female					
Diabetic (N = 306)	45.7 ± 6.7	98 (32%)	208 (68%)	76.5 ± 12.4	29.9 ± 4.6	93 ± 9.2	124.5 ± 18.6	79.6 ± 12.2
Prediabetic (N = 1309)	44.1 ± 6.7	337 (25.7%)	972 (74.3%)	74.9 ± 11.9	29.5 ± 4.2	90.5 ± 9.4	116.4 ± 16.3	75.7 ± 12.2
Normal (N = 1708)	42.3 ± 6.5	430 (25.2%)	1278 (74.8%)	72.8 ± 12.5	28.4 ± 4.3	87.7 ± 9.8	113.5 ± 16.2	74.1 ± 12.1
Total (N = 3323)	43.4 ± 6.7†	865 (26%)	2458 (74%)*	73.9 ± 12.3†	29 ± 4.3†	89.4 ± 9.8†	115.6 ± 16.7†	75.2 ± 12.2†

Values are expressed as mean ± SD or number (%).
$^{\dagger}p < 0.001$; $^{*}p = 0.04$
BMI: Body mass index; BP: Blood pressure

Table 2. Results of post hoc tests (p values) for continuous variables among diabetic (D), prediabetic (Pre) and normal (N) groups

	D and N	Pre and N	D and Pre
Age (year)	< 0.001	< 0.001	0.001
Weight (kg)	< 0.001	< 0.001	0.114
Body mass index (kg/m^2)	< 0.001	< 0.001	0.478
Waist Circumference (cm)	< 0.001	< 0.001	< 0.001
Systolic blood pressure (mmHg)	< 0.001	< 0.001	< 0.001
Diastolic blood pressure (mmHg)	< 0.001	0.002	< 0.001

Table 3. Demographic, anthropometric and clinical characteristics of diabetic, prediabetic and normal participants by gender

	Sex	Age (year)	Weight (kg)	BMI (kg/m2)	Waist circumference (cm)	Systolic BP (mmHg)	Diastolic BP (mmHg)
Diabetic	*Male* **(N = 98)**	46.7 ± 6.6	80.9 ± 12.8	28.2 ± 3.7	97.2 ± 8.2	125.2 ± 21.8	80.7 ± 12.5
	Female **(N = 208)**	45.3 ± 6.7	74.4 ± 11.7	30.7 ± 4.7	92.1 ± 9.3	124.1 ± 16.9	79.1 ±12.0
Prediabetic	*Male* **(N = 337)**	44.4 ± 6.9	80.6 ± 10.7	28.2 ± 3.3	95.8 ± 8.1	117.7 ± 14.8	77.5 ± 12.0
	Female **(N = 972)**	44 ± 6.7	72.9 ± 11.6	30 ± 4.5	88.9 ± 9.2	115.9 ± 16.7	75.1 ± 12.2
Normal	*Male* **(N = 430)**	43 ± 7.1	79.3 ± 13.2	27.1 ± 3.6	93.4 ± 9.4	116.4 ± 16.6	76 ± 12.5
	Female **(N = 1278)**	42.1 ± 6.3	70.6 ± 11.5	28.9 ± 4.4	85.9 ± 9.2	112.5 ± 16.0	73.4 ± 11.9
Total	*Male* **(N = 865)**	44 ± 7.1†	80 ± 12.2*	27.7(3.5)†	94.8 ± 8.9†	117.9 ± 1.7†	77.1 ± 12.3**
	Female **(N = 2458)**	43.2 ± 6.6†	71.8 ± 11.7†	29.5(4.5)†	87.6 ± 9.4†	114.8 ± 16.7†	74.5 ± 12.1†

Values are expressed as mean ± SD.
†p < 0.001; *p = 0.266; **p = 0.003
BMI: Body mass index; BP: Blood pressure

Table 4. Results of post hoc tests (p values) for continuous variables among diabetic (D), prediabetic (Pre) and normal (N) groups by gender

	D and N		Pre and N		D and Pre	
	Male	Female	Male	Female	Male	Female
Age (year)	< 0.001	< 0.001	0.029	< 0.001	0.016	0.041
Weight (kg)	0.518	< 0.001	0.357	< 0.001	0.978	0.212
Body mass index (kg/m^2)	0.023	< 0.001	< 0.001	< 0.001	0.996	0.147
Waist Circumference (cm)	0.001	< 0.001	0.001	< 0.001	0.393	< 0.001
Systolic blood pressure (mmHg)	< 0.001	< 0.001	0.558	< 0.001	0.001	< 0.001
Diastolic blood pressure (mmHg)	0.004	< 0.001	0.28	0.006	0.084	< 0.001

In prediabetic subjects, the male and female subgroups were identical regarding mean age and systolic blood pressure (p = 0.424 and p = 0.075, respectively). However, significant differences were observed in mean values of weight, BMI, waist circumference and diastolic blood pressure between the two subgroups (p < 0.00.1 for weight, BMI and waist circumference; p = 0.002 for diastolic blood pressure). Among participants with normal glucose tolerance test results, the existing differences in age, weight, BMI, waist circumference, systolic and diastolic blood pressures between males and females were all significant (p = 0.021 for age; p < 0.001 for other variables).

Table 5 shows the prevalence of normal weight, overweight and obesity in the three studied groups by sex. In diabetic patients, the prevalence of obesity was 48.6% in women and 27.6% in men (p = 0.001). Among prediabetics, the corresponding figures were 45.6% and 27.3%, respectively (p < 0.001).

In diabetic patients, the BMI of 92.4% of females and 85.8% of males was greater than 25 kg/m^2 (p = 0.098). In prediabetic individuals, 88.1% of females and 86.4% of males had a BMI of > 25 kg/m^2 (p = 0.442). In participants with normal glucose tolerance, the corresponding figures were 82.7% and 73.7%, respectively (p < 0.001).

DISCUSSION

Our study on first degree relatives of T2DM patients revealed a considerably high prevalence of overweight and obesity among prediabetic and diabetic individuals. Of special concern was the significantly higher prevalence of weight disorders in women than in men.

Although the group studied in the current survey were genetically prone to diabetes, but a high prevalence of overweight and obesity was documented among individuals affected with prediabetes and diabetes. This finding underscores the importance of prevention and early control of excess weight in populations at risk for T2DM. Obesity and T2DM are multifactorial health conditions caused by a complex genetic-environment interaction. Nevertheless, the role of modifiable lifestyle factors on weight status is well documented.[27,28] Therefore, the fundamental role of lifestyle factors in the development of diabetes should be considered in preventive strategies. Two strategies have been proposed in this regard. The population strategy seeks to eliminate the causes of disease in populations as a whole, whereas the high-risk strategy aims to recognize persons at increased risk, and to consider individual interventions. However, controversies exist about the cost-effectiveness of the

Table 5. The prevalence of normal weight, overweight and obesity in diabetic, prediabetic and normal groups by gender

Sex		Body mass index* (kg/m2)		
		< 25 (Normal weight)	25-29.99 (Overweight)	≥ 30 (Obese)
Diabetic	*Male* **(N = 98)**	14 (14.3%)	57 (58.2%)	27 (27.6%)
	Female **(N = 208)**	16 (7.7%)	91 (43.8%)	101 (48.6%)
	Total[*] **(N = 306)**	30 (9.8%)	148 (48.4%)	128 (41.8%)
Prediabetic	*Male* **(N = 337)**	46 (13.6%)	199 (59.1%)	92 (27.3%)
	Female **(N = 972)**	116 (11.9%)	413 (42.5%)	443 (45.6%)
	Total[**] **(N = 1309)**	162 (12.4%)	612 (46.8%)	535 (40.9%)
Normal	*Male* **(N = 430)**	113 (26.3%)	234 (54.4%)	83 (19.3%)
	Female **(N = 1278)**	222 (17.4%)	604 (47.3%)	452 (35.4%)
	Total[**] **(N = 1708)**	335 (19.6%)	838 (49.1%)	535 (31.3%)

Values are expressed as number (%).
[*] p = 0.002; [**] p < 0.001

high-risk approach. Our findings are consistent with a recent review highlighting the role of lifestyle factors in the development of diabetes. This review clarified that most of the genes identified to date, have modest effect on disease risk, and suggested that obesity and diabetes are not likely to develop without exposure to obesogenic environment. Thus, irrespective of genetic susceptibility, healthy lifestyle may be helpful in preventing diabesity. However, due to individual response to a lifestyle intervention program, individualized interventions according to genotype may be considered in the future.[29]

The national estimates of overweight and obesity in Iran are 28.6% and 14.2%, respectively. Excess weight is mainly reported among women with a prevalence of 48% for overweight and 43.4% for abdominal obesity.[22,23] Given that in our community, sedentary lifestyle is known as the major contributing factor for the emergence of this public health problem,[22] increasing public awareness in this regard may have long-term health impacts.

We found that among diabetic patients, the mean BMI was lower in men than in women. This finding is consistent with a study in Scotland which showed T2DM men to have lower BMI than women. The study considered this gender difference as one of the main reasons of the high prevalence of T2DM among middle-aged European men. It thus suggested studying this pattern in other ethnic groups.[30] Our findings may serve as a confirmatory evidence of this pattern in a Middle-Eastern population.

Study limitations and strengths:

The main limitation of our study was its cross-sectional nature which made the determination of causative effects impossible. A follow-up study of the same population will be of help in this regard. The main strength of this study was enrollment of a large sample size of the first-degree relatives of diabetic patients, as a group at-risk for disorders of glucose metabolism.

Conclusion

Excess weight has a fundamental role in the development of dysglycemia and diabetes among the first degree relatives of diabetic patients. Our findings suggest that men are diagnosed with T2DM at lower BMI than women. Moreover, the alarming high prevalence of overweight and obesity among females necessitates preventing and controlling this underlying problem among females. Relatives of T2DM patients shall be considered as the primary target population for diabetes prevention programs.

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