Original Article

Changes in Body Weight and Fat Distribution; Risk Factors for Abnormal Glucose Homeostasis? Tehran Lipid and Glucose Study

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Abstract

Background: Obesity is a known risk factor for type 2 diabetes and its prevalence is increasing. The aim of this study was to examine the association between changes in body weight and body fat distribution and the subsequent risk of pre-diabetes and/or diabetes over a 3-year period among a population of Tehran Citizenry.
Methods: A total of 3957 subjects aged 20 years and over, participants of the Tehran Lipid and Glucose Study, were included in this study. Demographic characteristics, plasma glucose in both the fasting state and two hours after 75gr oral glucose were measured at baseline (1998-1999) and after 3 years (2001-2002). Subjects were divided according to their baseline body mass index (BMI), weight changes (loss > 4%, loss or gain < 4%, 4-10% and > 10% weight gain), quintile of changes in waist circumference (WC) and waist to hip ratio (WHR) over the study period. The relative risk of developing pre-diabetes and/or diabetes was measured after adjustment for age, sex and family history of diabetes.
Results: After three years of follow-up, 3.7% developed diabetes. Weight gain and baseline BMI were related to risk of developing pre-diabetes or diabetes in subjects with normal plasma glucose. Compared with subjects with stable weight, those who gained weight by 4-10% and >10% had 1.2 (1.01-1.53) and 1.3 (1.04-1.86) times the risk of pre-diabetes or diabetes, respectively after controlling for age, sex, family history of diabetes and BMI. In contrast, participants who lost >4% in weight, the relative risk decreased significantly [RR: 0.4 (0.27-0.65)]. These effects of weight changes were seen mostly in female subjects. Also, according to the baseline BMI, the risk increased in overweight and obese subjects by 1.7 (1.36-2.40) and 2.0 (1.55-2.63) times, respectively. Individuals with pre-diabetes at baseline, only BMI ≥ 30 kg/m^2 was associated with the increased risk of diabetes [RR: 2.7 (1.49-4.78)]. There was no relation between changes in WC or WHR and risk of developing abnormal glucose homeostasis after controlling for BMI and weight gain.
Conclusion: Weight gain and BMI were independent risk factors in the development of abnormal glucose homeostasis. The data support public health recommendations to reduce the risk of diabetes by preventing weight gain and encouraging weight loss in overweight and obese People.

Keywords*:* Body mass index, waist circumference, Waist/Hip ratio, Obesity, Diabetes, Prediabetes

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Introduction

As a result of industrialization and related sedentary lifestyles, obesity has become a major health problem, especially in the industrialized countries. Obesity not only causes insulin resistance and glucose intolerance, but also exacerbates associated metabolic abnormalities [1].

The progression of patients with pre-diabetes to a diagnosis of type 2 diabetes ranges from 5% to 10% per year, depending on the genetic predisposition [2]. Stengard et al. [3] evaluated the natural history of glucose tolerance during a five-year follow-up among elderly Finnish men. At baseline, of the 637 men, 216 had normal and 234 had impaired glucose tolerance (IGT), and 187 were diabetic. At follow-up, 18% of the subjects with normal glucose tolerance at baseline had either IGT or diabetes; 7% of the men with initially IGT had developed diabetes, and 34% were normal. 13%` and 12% of the initially diabetic subjects had reverted to impaired or normal glucose tolerance, respectively. The age in the Stengard study was able to explain 1-2% of variation in blood glucose level in cross-sectional but not in longitudinal comparison. Body mass index (BMI) was an important predictor of abnormal glucose tolerance test in previously normal responding men. By contrast, obesity did not contribute to the development of diabetes among men with IGT. In the study by Chou P et al. [4], 481 subjects (53% men) were followed up for 3-4 years. Of these, 8.1% had progressed to diabetes (4.1% progression/year, 95% CI: 2.3 -5.9). Of 131 baseline IGT subjects, 17.6% progressed to diabetes (8.8% progression/ year, 95% CI: 6.3-11.3), but only 7.4% of 95 subjects with persistent fasting hyperglycemia (3.7% progression/year, 95% CI: 2.0-5.4) and 3.5% of 255 subjects with normal glucose tolerance (1.8% progression/ year, 95% CI: 0.1-3.0) progressed to diabetes. Meigs JB et al. [5] also studied the natural history of progression from normal glucose tolerance (NGT) to type 2 diabetes. Of the 488 subjects with NGT, 43% progressed to impaired fasting glucose (IFG) and 43% to IGT within 10 years of follow-up; among subjects developing IFG or IGT, 22% progressed to diabetes by IFG whereas 17% progressed to IGT within 10 years. Nonetheless, 42% of subjects developing IFG did not develop IGT, and vice versa.

According to the results of the first phase of the Tehran Glucose and Lipid Study (TLGS), among people over 20 years of age, the prevalence of overweight and obesity were 40 and 23% and the prevalence of impaired glucose tolerance and diabetes were 12.4 and 10.6%, respectively [6]. Considering the high rates of overweight/obesity and glucose intolerance/diabetes, and there is no study in Iran that has studied the trend of weight changes and glucose intolerance prospectively, accordingly this study was carried out with the aim of examining the effects of weight change and body fat distribution on the blood glucose status, three years after the beginning of TLGS.

Methods

Study Population

The TLGS, an epidemiological study to estimate the prevalence and incidence of metabolic disorders and the risk factors of non-communicable diseases (NCD) is being conducted among residents of 13th district 13 of Tehran [6, 7]; its aim is to change lifestyles to prevent major NCDs'. The design of this study encompasses two major components, the first phase, a cross-sectional prevalence study of cardiovascular diseases and associated risk factors and the second phase, a prospective follow-up study for 20-years. A multistage stratified cluster random sampling technique was used to recruit 15005 people, aged 3 years or older, from 13th district of Tehran. From this population, normal and pre-diabetic (including IFG and IGT) individual, older than 20 years, who participated both in phase 1 in 1998-1999 and phase 2 in 2001-2002 were chosen. The interval between two assessments was approximately 3 years. Individuals who were taking medications affecting blood glucose (such as corticosteroid, diazoxide, pentamidine, alpha interferon, phenytoin, thiazides, nicotinic acid, beta agonists or blockers, thyroidal hormones, quinine, somatostatin analogs) or had a history of diseases that could affect blood glucose (such as cushing's syndrome, acromegaly, hyperthyroidism, pheochromocytoma) were excluded. Finally 3957 subjects were studied.

Anthropometric measures

Data relating to medical history and drugs consumption were recorded by a physician. Anthropometric data such as height, weight, hip and waist circumferences (WC) were measured by a trained person. Weight was measured using a digital electronic weighing scale (Seca 707, anthropometric and clinical, range 0.1 to 150 kg) without shoes or additional clothes, with ±100 grams accuracy. Height was measured without shoes, in standing posture, by a tape meter stadiometer with 1 mm accuracy. The body mass index (BMI) was calculated by dividing weight (kg) to the square of height (m^2). Waist and hip circumferences were measured using the standard protocols and waist to hip ratio (WHR) [waist circumference (cm)/hip circumference (cm)] was calculated. In the first phase of the study, the digital preference scores (DPI) [8] for measurement of height, weight and waist circumference in men were 2.1, 1.84, 1.88, and for women, 1.82, 3.17 and 5.73, respectively. In the second phase of the study of the overall DPI for measurement of height, weight and waist circumference were 1.13, 1.58 and 3.45, respectively.

From among the studied individuals, information regarding WC and the WHR were available in 3,768 cases. Of these 2,897 had normal blood sugar and 870 were prediabetic. The individuals in each group were divided into five categories according to the quintile of percentage of changes in WC and the WHR, and the relative risk was calculated after the following adjustments: 1) for age, 2) for age, sex, family history of diabetes and the baseline BMI (continuous) in the first year of the study, and 3) after further adjustment for weight changes (continuous) during the three years of follow-up.

The individuals were also categorized according to their baseline BMI (low weight <18.5, normal weight 18.5-24.9, overweight 25-29.9, and obese ≥30 kg/m^2) [9], and in each group, the weight changes (weight loss > 4% baseline weight, stable weight equal to ± 4% baseline weight, gain of 4-10% of baseline weight and weight gain >10% of baseline weight) and changes in blood glucose were calculated between the two phases.

Laboratory Methods

After 12-14 hours fasting, 10 ml of venous blood sample was taken for measurement of fasting plasma glucose (FPG) and another sample was taken for blood sugar 2 hours after consuming 75 grams of oral> glucose. A standard oral glucose (C.f.a.s, Roche Germany) was used for the oral glucose tolerance test. All blood analyses were performed in the laboratory of the endocrine research center. The blood glucose was measured using the glucose kits of Pars Azmoun Co., Iran, with the enzymatic calorimetric method and with the oxidase glucose technology. The coefficient of variation for glucose measurement in phase 1 was 2.3% and in phase 2 was 2.4%.

The subjects were divided according to their blood glucose status into three groups: normal, pre-diabetic and diabetic [10]. The categories of FPG values are as followed: FPG <100 mg/dl = normal fasting glucose; FPG 100–125 mg/dl = impaired fasting glucose (IFG); FPG ≥126 mg/dl = provisional diagnosis diabetes (the diagnosis must be confirmed, as described below). The peer categories when the OGTT is used are as followed: 2-h postload glucose <140 mg/dl = normal glucose tolerance; 2-h postload glucose 140–199 mg/dl = impaired glucose tolerance (IGT); 2-h postload glucose ≥200 mg/dl= provisional diagnosis of diabetes. In the absence of unequivocal hyperglycemia, these criteria confirmed by repeat testing on a different day.

Patients with IFG and/or IGT are now referred to as having "pre-diabetes".

Statistical Methods

Data were analyzed by using the SPSS software (Version 11.00; SPSS, Inc., Chicago Ill., USA). The baseline variables in different groups of blood glucose status were after three years compared using the ANOVA. The X^2> test was used for comparing the BMI between two phases of the study. The Cox regression model was used for calculating the relative risk of developing prediabetes and diabetes in different groups relative to the changes in weight, WC and WHR, and the results were adjusted according to age, sex and family history of diabetes.

This study was approved by the Research Ethics Committee of the Endocrine and Metabolism Research Center of Shahid Beheshti University of Medical Sciences and informed consent was obtained from all subjects.

Results

In this study, 3957 people were recruited, of whom 43.3% were male. The mean age of the men and women in the beginning of the study was 44.3±14.2 and 40.3±12.4 years, respectively. At baseline nearly three quarter of subjects had normal glucose status and the remaining were prediabetic (Table 1). From the study population, after 3 years, 3.7% had developed diabetes; most of them had shifted from prediabetes to diabetes rather than from normal blood glucose to diabetes (lower than 1/5 of all the cases). Eighty four percent of normal and 48% of prediabetic individuals had no changes in their blood glucose status. Fifteen% of normal subjects became pre-diabetic, of which approximately 1% developed diabetes.

The baseline characteristics of the studied individuals based on the blood glucose status after three years of follow-up are shown in Table 2. There are no significant differences between the groups in terms of sex. However, the mean age of the individuals having a normal blood glucose (40.1±13.1 years) was significantly ($P<0.001$) lower than that of the prediabetic (47.4±12.8 years) and diabetic individuals (47.8±12.4 years). The baseline BMI, weight, WC and WHR in individuals with normal blood glucose after three years were significantly lower than those who had developed prediabetes or diabetes. However, there was no significant difference between the three groups regarding weight changes after 3-years. In addition, the baseline BMI and WC in individuals who developed pre-diabetes was significantly lower than those who had became diabetic. The family history of diabetes in the group has developed diabetes was significantly greater than the other two groups.

Effects of the BMI and Weight Changes:

A comparison of BMI in individuals at the beginning of the study and three years after follow-up showed that the weight of the individuals in each weight group increased significantly (Table3). In individuals with normal blood glucose the relative risks of developing of prediabetes or diabetes, in men and women respectively, in the overweight group were 1.8 (95% CI:1.34-2.49) and 1.5 (95% CI:1.09-2.13), and in the obese groups, were 2.1 (95% CI:1.43-3.21) and 1.8 (95% CI:1.26-2.59) in comparison to individuals with a normal baseline MBI. When the effect of the high BMI in all individuals with normal blood sugar was examined after further adjustment for sex (Table 4) the relative risk of developing of prediabetes or diabetes was 1.7 (95% CI: 1.36-2.40) in the overweight group and 2.0 (95% CI: 1.55-2.63) in the obese subjects.

Table 1. Comparison of blood glucose status of the study subjects at baseline and at end of study

	Baseline	After three years follow-up		
		Normal	Prediabetes	Diabetes
Normal†	3046 (77)	2560 (84)	459 (15.1)	27 (0.9)
Prediabetes†	911 (23)	348 (38.2)	442 (48.5)	121 (13.3)

† Number in parenthesis denote percent; * P<0.001

Table 2. Baseline characteristics (mean ± SD) of the study subjects according to their blood glucose status at end of study

Baseline characteristics	After three years follow-up		
	Normal	Prediabetes	Diabetes
Number of cases†	2908	901	148
Age (yr)	40.1 ± 13.1	47.4 ± 12.8	47.8 ± 12.4
Male (%)	42.4	46.3	43.9
BMI (kg/m^2)	26.2 ± 4.2 *	28.2 ± 4.5 **	29.2 ± 4.4
Weight (kg)	69.5 ± 12.4 *	74 ± 13.1	76.3 ± 13.5
Weight changes (kg)	2.1 ± 4.7	2.2 ± 4.4	2.2 ± 5.1
Waist circumference (cm)	86.1 ± 11.3 *	92.1 ± 10.9 ***	95.7 ± 10.2
Waist/Hip ratio (WHR)	0.85 ± 0.08 *	0.9 ± 0.08	0.9 ± 0.08
Family history of diabetes (%)	24.8 *	29.7 ***	48.6

* P<0.001 in comparison with prediabetes and diabetes; ** P<0.04 and ***P<0.001 in comparison with diabetes
† At the beginning of the study 3046 subjects had normal blood glucose and 911 subjects were prediabetic

Table 3. Comparison of body mass index of the study subjects at baseline and at end of study

Body mass index	Baseline†	After three years follow-up†
Low weight (<18.5 kg/m^2)	85 (2.2)	42 (1.1)*
Normal weight (18.5-24.9 kg/m^2)	1263 (33.3)	1012 (26.7)*
Overweight (25-29.9 kg/m^2)	1583 (41.8)	1656 (43.7)*
Obese (> 30 kg/m^2)	858 (22.6)	1079 (28.5)*

† Number in parenthesis denote percent; * P< 0.001

Table 4. Relative risk and 95% confidence interval for prediabetes and diabetes by baseline body mass index and weight change after three years in subjects with normal blood glucose at baseline

Variables	No. of Cases	RR (95% CI)*	RR (95% CI)**
Baseline BMI (kg/m2)†			
< 18.5	68	0.6 (0.21-1.61)	0.6 (0.22-1.63)
18.5 – 24.9	1069	1.0	1.0
25 – 29.9	1209	1.7 (1.35-2.13)	1.7 (1.36-2.40)
≥ 30.0	560	2.0 (1.54-2.58)	2.0 (1.55-2.63)
Weight change after three years (%) ‡			
Loss of > 4%	265	0.4 (0.27-0.64)	0.4 (0.27-0.65)
Loss of 4% - Gain of 4%	1320	1.0	1.0
Gain of > 4 – 10 %	933	1.3 (1.02-1.54)	1.2 (1.01-1.53)
Gain of > 10 %	388	1.4 (1.03-1.85)	1.3 (1.04-1.86)

* Adjusted for Age; ** Adjusted for Age, Sex and Family history of diabetes
† Adjusted for Weight change (continuous) after three years; ‡ Adjusted for baseline BMI (continuous)

The relative risks of developing prediabetes or diabetes in women with 4-10% and >10% weight gain from the initial body weight during 3 years, after adjustment for age, family history of diabetes and the baseline BMI, were 1.6 (CI 95%:1.17-2.07) and 1.8 (CI 95%:1.23-2.64) respectively, as compared to that of the women with a stable weight. However, such an effect was not seen among male subjects. On the other hand, the relative risk of prediabetes or diabetes decreased with the loss of weight so that, in women and men with a weight loss of more than 4% of the initial body weight, the relative risk of prediabetes or diabetes was 0.6 (95% CI: 0.35-0.96) and 0.2 (95% CI: 0.09-0.54), respectively. When the effect of the weight changes in all of the studied subjects were examined after adjustment for sex, there was still a statistically significant relative risk of developing of prediabetes or diabetes in individuals with normal blood glucose (Table 4), so that the relative risk of prediabetes or diabetes in the group with a 4-10% and >10% weight gain of the initial weight during the 3 years after adjustment for age, sex, family history of diabetes and the baseline BMI was 1.3 (95% CI: 1.01-1.53) and 1.4 (95% CI: 1.04.-1.86), respectively as compared to that of the group with a stable weight. On the other hand, with weight loss, the relative risk of prediabetes or diabetes dropped, being 0.4 (95% CI: 0.27-0.65) in the group with a weight loss of more than 4% of the initial weight compared to the group with a stable weight. The effect of the weight changes on the risk of developing diabetes in prediabetic individuals, except for weight loss in women, which had a marginal effect [RR: 0.3 (95% CI: 0.09-0.99)], were not significant in any of the other groups (Table 5).

Increase in relative risk according to the BMI in prediabetic individuals was seen only in obese individuals (Table 5) so that, after adjustment for age, sex, family history of diabetes and weight changes within the three years, the relative risk of developing of diabetes was 2.7 (95% CI: 1.49-4.78). However, when this effect was examined according to sex, it was statistically significant only in women so that, in comparison with women with a normal baseline BMI, after adjustment for other confounding factors, the relative risk of developing of diabetes was 3.5 (95% CI: 1.21-10.06) in overweight and 4.6 (95% CI: 1.62-12.96) in obese women. The relative risk in the low baseline BMI was not statistically significant in the entire study population.

Effect of changes of waist circumference and the waist to hip ratio

Increase in waist circumference from the third to the fifth quintile compared to those with a relatively stable WC within the three years (second quintile) after adjustment for age, sex, family history of diabetes and the BMI had significantly ($P<0.001$) increased the relative risk of the development of prediabetes or diabetes in individuals with normal blood sugar and yet this was not statistically significant anymore after further adjustment for weight changes (Table 6). Such an effect was not seen in the other groups with normal blood sugar (men and women, separately or the entire study population).

For changes of WC in prediabetic individuals, only reduction in waist circumference in the first quintile compared to those with a relatively stable WC within the three years (the second quintile) had significant effect. The relative risk of developing diabetes in men after adjustment for age, family history of diabetes and the baseline BMI [0.4 (95% CI: 0.14-0.98)] and in women after adjustment for age [0.4 (95% CI: 0.18-0.97)] or age, sex, family history of diabetes and the baseline BMI [0.4 (95% CI: 0.17-0.95)] were only marginally statistically significant and yet this was not significant anymore after further adjustment for changes of weight in any of the sex groups or in the entire study population after adjustment for sex (Table 7).

Table 5. Relative risk and 95% confidence interval for diabetes by baseline body mass index and weight change after three years in subjects with prediabetes at baseline

Variables	No. of Cases	RR (95% CI)*	RR (95% CI)**
Baseline BMI (kg/m2)†			
< 18.5	6	-	-
18.5 – 24.9	194	1.0	1.0
25 – 29.9	347	1.9 (1.01-3.52)	1.8 (0.97-3.20)
≥ 30.0	298	2.9 (1.61-5.14)	2.7 (1.49-4.78)
Weight change after three years (%) ‡			
Loss of > 4%	129	0.6 (0.28-1.10)	0.5 (0.27-1.05)
Loss of 4% - Gain of 4%	485	1.0	1.0
Gain of > 4 – 10 %	186	1.4 (0.95-2.17)	1.5 (0.95-2.20)
Gain of > 10 %	72	0.8 (0.38-1.59)	0.8 (0.37-1.57)

* Adjusted for Age; ** Adjusted for Age, Sex and Family history of diabetes
† Adjusted for Weight change (continuous) after three years; ‡ Adjusted for baseline BMI (continuous)

Table 6. Change in waist and waist/hip ratio (WHR) after three years as risk factors for prediabetes/diabetes in subjects with normal blood glucose at baseline

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	***P* for trend**
Waist change after three years						
No.	654	508	589	562	585	
Range (%)	-0.48 to 0.008	0.009 to 0.039	0.04 to 0.075	0.076 to 0.117	> 0.118	
Adjusted for Age	0.8 (0.58 - 1.12)*	1.0	1.3 (0.97 - 1.74)	1.3 (0.94 - 1.70)	1.3 (0.99 - 1.79)	0.05
Multivariate Adjusted †	0.8 (0.59 - 1.14)	1.0	1.4 (1.01 - 1.81)	1.4 (1.02 - 1.86)	1.6 (1.18 - 2.16)	0.001
Multivariate Adjusted ‡	0.9 (0.65 – 1.26)	1.0	1.3 (0.98 - 1.76)	1.3 (0.92 - 1.71)	1.3 (0.97 - 1.85)	0.07
WHR change after three years						
No	578	581	580	580	579	
Range (%)	-0.44 to -0.112	-0.113 to 0.022	0.023 to 0.049	0.05 to 0.085	> 0.085	
Adjusted for Age	0.9 (0.63 – 1.16)	1.0	1.2 (0.89 - 1.56)	1.1 (0.81 - 1.45)	1.03 (0.77 - 1.37)	0.3
Multivariate Adjusted †	0.8 (0.61 – 1.15)	1.0	1.2 (0.94 - 1.65)	1.1 (0.82 - 1.46)	1.1 (0.84 - 1.51)	0.1
Multivariate Adjusted ‡	0.8 (0.62 – 1.16)	1.0	1.2 (0.90 - 1.59)	1.03 (0.77 - 1.37)	1.02 (0.75 - 1.37)	0.2

*Relative Risk (95% Confidence Interval)
†Adjusted for Age, Sex, Family history of diabetes and Baseline BMI (continuous) ; ‡ After further adjustment for Weight change (continuous) after three years

Table 7. Change in waist and waist/hip ratio (WHR) after three years as risk factors for diabetes in subjects with prediabetes at baseline

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	***P* for trend**
Waist change after three years						
No.	173	176	172	176	173	
Range (%)	-0.34 to -0.01	-0.009 to 0.025	0.026 to 0.053	0.054 to 0.091	> 0.091	
Adjusted for Age	0.6 (0.35 - 1.18)*	1.0	0.8 (0.45 - 1.39)	1.2 (0.69 - 1.96)	0.6 (0.32 - 1.03)	0.09
Multivariate Adjusted †	0.5 (0.29 - 1.01)	1.0	0.7 (0.43 - 1.33)	1.2 (0.71 - 2.03)	0.6 (0.33 - 1.08)	0.05
Multivariate Adjusted ‡	0.6 (0.32 – 1.17)	1.0	0.8 (0.42 - 1.31)	1.1 (0.65 - 1.91)	0.5 (0.27 - 0.98)	0.05
WHR change after three years						
No.	174	174	174	174	174	
Range (%)	-0.31 to -0.02	-0.019 to 0.013	0.014 to 0.039	0.04 to 0.078	> 0.078	
Adjusted for Age	1.06 (0.60 – 1.87)	1.0	1.06 (0.60 - 1.85)	0.9 (0.49 - 1.67)	0.9 (0.47 - 1.54)	0.9
Multivariate Adjusted †	0.9 (0.53 – 1.68)	1.0	1.2 (0.67 - 2.05)	0.9 (0.51 - 1.71)	0.9 (0.48 - 1.57)	0.9
Multivariate Adjusted ‡	1.03 (0.58 – 1.83)	1.0	1.2 (0.67 - 2.05)	0.9 (0.52 - 1.73)	0.8 (0.44 - 1.47)	0.8

*Relative Risk (95% Confidence Interval)
†Adjusted for Age, Sex, Family history of diabetes and Baseline BMI (continuous) ; ‡ After further adjustment for Weight change (continuous) after three years

In addition, concerning changes in WHR, no significant effect was seen in any of the groups of individuals with normal blood sugar or prediabetes (men and women separately, or all individuals as a whole).

Discussion

The findings of this study confirm increase in the prevalence of obesity and overweight state in individuals aged over 20 years in the urban community of Tehran. Such a growing trend can be seen in each of the weight groups and the entire studied population; 64.4% in the beginning of the study to 72.2% after three years.

After three years of follow-up, 15% and nearly 1% of individuals with normal blood glucose became pre-diabetic and diabetic, respectively and in prediabetic individuals,

13% had developed diabetes and in 38%, blood glucose status became normal.
Obesity is the most apparent manifestation of the increase in calorie intake and sedentary lifestyle. Estimated prevalence of obesity varies worldwide [11]. According to the reports from different regions of the world, the prevalence of obesity is increasing in both developed and developing countries. It is reported that 13% of men and 14% of women in Canada are obese [12]. In European countries, prevalence ranges from 10 to 20% among men and 10-25% among women [13]. In Australia, 9% of men and 11% of women [14] and in the United states , 20% of men and 25% of women are considered obese [15].
Obesity is one of the most important risk factors for diabetes. Its risks have already been documented in several studies [16-20]. According to the recent survey in the United States, the risk of diabetes increased approximately 4.5% with every kilogram increase in measured weight. Such a relation existed in all age, sex and race groups [20].
It seems that, in Iran also, urbanization and lifestyle in cities, which contribute to the tendency towards inactivity, are among the factors that increase weight gain and obesity.
Such a growing trend can also be seen in blood glucose abnormalities. In this study, after three years, 26.5% of individuals were prediabetic or diabetic. Age, baseline BMI, weight, family history of diabetes, WC and WHR in those with normal blood sugar at the end of the study, were significantly lower than in individuals who had developed prediabetes or diabetes. However, in terms of sex and weight changes, no significant differences were seen between the groups. In this study it was seen that, after adjustment for age, sex, family history of diabetes and the baseline BMI, the relative risk of developing prediabetes or diabetes increases with further weight gain. On the other hand, with weight loss > 4% of the initial weight, this risk drops by 50%. This finding is in accordance to that of the DPP[1], in which, lifestyle intervention and reduction of at least 7% of the initial body weight, the incidence of diabetes reduced by 58% [21]. In addition, the higher the baseline BMI, the greater the increase in the relative risk of developing of prediabetes or diabetes, independent of weight changes. It seems that the small sample size statistically distorted the effect of the lower BMI on the relative risk of weight loss in this study. However, in the case of development of diabetes in prediabetic individuals, only a BMI >30 kg/m^2 significantly increased the relative risk of developing of diabetes and the effects in the other BMI groups and also the changes of weight were not statistically significant, which may be due to the small sample size and the short period of follow-up.
The findings of the present study are in agreement with those of other studies. In the study by Koh-Banerjee et al. [16], the mean weight change between 1986 and 1996 was approximately 1.8 ± 5.2 kg. Among men with the greatest weight loss (≥ 6 kg) over that period, the risk for developing of diabetes after adjustment for other confounding factors, reduced by approximately 50% compared to men whose weight remained stable (± 2 kg). On the other hand, this risk in those with 3-5 kg weight gain was 1.4 times, in those with 6-9 kg weight gain was 1.6 times and in those with ≥ 9 kg weight gain was 2.1 times higher. In addition, with a BMI > 23 kg/m^2, the risk of developing of diabetes increased. The relative risk for diabetes in individuals with a BMI of 23-24.9 kg/m^2 was 1.5, in those with a BMI of 25-29.9 kg/m^2 was 2.6 and in those with a BMI of ≥ 30 kg/m^2 were 4.9.
In the study by McNeely et al. [17] on 466 Japanese Americans, aged 34 to 75 years (52.4% men), the effect of weight changes, since the age of 20 yr, on the risk of developing of diabetes was studied. The mean weight change was 6.4 ± 0.3 kg

1 –Diabetes Prevention Project

(+11.5% of initial weight) and the mean weight gain in the group having developed diabetes was significantly [4.5% (P= 0.014)] more than the group that had remained non-diabetic. In the study by Wannamethee et al. [18], on 6916 Englishmen, 40-59 years of age, the risk of the development of diabetes was studied for a period of 12 years. In this study, the relative risk of developing of diabetes in the group with a weight loss of ≥4% of the initial body weight compared to the group with a stable weight was 0.66. It was 1.21 in the group with a weight gain of 4%-10% and 1.81 in the group with ≥10% of initial body weight. In the Nurses' Health Study by Colditz et al. [19], carried out on 114,824 women, 30-50 years of age, the relative risk of developing diabetes was 12.3 with weight gain of ≥ 20 kg, 5.5 with a weight gain of 11-19.9 kg, 2.7 with a weight gain of 8-10.9 kg and 1.9 with a weight gain of 5-7.9 kg. Also, in this study, after adjustment for age and weight changes, the greater the BMI > 22 kg/m^2, the greater the relative risk of developing of diabetes.

According to the results of studies in Iran, both a higher BMI and weight gain are independent risk factors for developing of blood glucose abnormalities in the future.

Abdominal obesity, which is evaluated by measuring the WC and WHR, is a component of metabolic syndrome, which accompanies blood glucose abnormalities [22]. In some studies, basal WC and WHR [23, 24] and their increment have shown a moderate association with the risk of development of type 2 diabetes in the future [16].

In the present study, increase in WC from the third quintile upward, after adjustment for age, sex, family history of diabetes and the basal BMI, significantly increased the risk of development of prediabetes or diabetes in individuals with normal blood glucose after three years of follow-up. However, after further adjustment for weight changes, it was not statistically significant anymore. In these individuals, changes of WHR did not have any significant effects on the risk of development of blood glucose abnormalities. Also in prediabetic individuals, after adjustment for age, sex, family history of diabetes, initial BMI and weight changes after three years, neither change in WC nor in WHR had any statistically significant effect on development of diabetes. These findings were inconsistent with the previous studies, the reasons for which may be that the BMI and the changes of weight had more effect on development of blood glucose abnormalities and this surpassed the effects of the increase of the WC or WHR. Also in our population, the effect of changes in the WC and WHR on blood glucose abnormalities may differ from other ethnic groups. Verification of this hypothesis requires a study with a larger sample size and longer duration.

The limitations of the present study include a drop in the number of individuals participating in the second phase of the study (44%) and lack of accessibility to or incomplete information given by some individuals participating in the second phase of the study. Therefore, some individuals were excluded in the analysis, thus making a small sample size in some groups. In addition, the duration of follow-up was somewhat shorter than other studies; the present study may however provide the groundwork for more precise studies in the future.

In conclusion, this 3-year follow-up of the TLGS indicates a growing trend in overweight state, obesity, glucose intolerance and diabetes in our society. It is recommended that people be made more socially aware through mass media and health care providers with a view to encouraging them to reduce their weight using life style changes; this in turn would result in a decrease in insulin resistance and a delay or prevention in development of glucose intolerance, diabetes and related complications, and eventually a much warranted control in burden of the disease.

Acknowledgments

The authors are grateful to the director and personnel of the research department and the statisticians of the Endocrine and Metabolism Research Center of Shaheed Behehsti University of Medical Sciences for financial support and cooperation throughout this study.

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