Iranian J Publ Health, Vol. 42, No.7, July 2013, pp.681-690

Original Article

Type 2 Diabetes Family Histories, Body Composition and Fasting Glucose Levels: A Cross-Section Analysis in Healthy Sedentary Male and Female

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(Received 24 Feb 2013; accepted 18 Jun 2013)

Abstract

Background: Diabetes type 2 is a world wide spread disease with a multifactorial pathogenetic evolution. Various factors like obesity, physical inactivity and poor lifestyle habits contribute to its development. The aim of this study was to verify if in young healthy sedentary male and female there is positive correlation between family history to type 2 diabetes and an increase in body weight and fat mass, or alterations in basal glycemia values.

Methods: Totally183 male and 237 female healthy sedentary subjects were analysed in 2012, in Italy. They were divided in three groups: FH^{+} with first degree family history, $FH^{++}$with second degree family history and FH^{-} with no family history. Anthropometrics, body composition and blood parameters were assessed.

Results: Male had the highest BMI values ($P<0.01$). FH^{+} and FH^{++} had increased waist and hip circumferences and body weight ($P<0.005$ for men, $P<0.0001$ for women), body mass index ($P< 0.0001$ in both sexes), waist-hip ratio ($P< 0.05$ for men and women) and triceps skinfold ($P< 0.0005$ for both sexes). Obesity incidence was higher in FH^{+} and FH^{++} compared to control groups.

Conclusions: The study confirms family history to diabetes type 2 as a risk factor for the development of the illness, mainly in a case of first degree of FH. Preventive interventions are necessary to promote significant life-style changes, such as increased physical activity and controlled quantity and quality of food intake.

Keywords: Lifestyle, Fasting glucose level, Type 2 diabetes, Family history, Body composition.

Introduction

A deficit in insulin secretion and physiological tissutal action induces mellitus diabetes, causing chronic hyper-glycemia and various metabolic diseases(1).In occidental industrialized countries, type 2 diabetes (TD2) is the most widely spread disease, showing a constant increase of incidence also in young population. Moreover, genetic and environmental risk factors influence diabetes development: family history, age, obesity and physical inactivity (2).Maternal influence confirmed the hereditary role in the diabetes pathogenesis: women with positive family history to the illness presented major risks to develop gestational TD2, confirming the inter-generative transmission of this disease(3-11). Further studies showed the precocious influences of positive family history to TD2 on subjects' phenotype, generating an in-

crease in body weight and a tendency towards obesity and visceral adiposity (12-16).
Other studies showed metabolic disorders related to a positive family history to TD2: glucose metabolic disorders, insulin-resistance, an increase in blood pressure and a reduced glucose tolerance (9, 11, 14, 17-20).
Even energy expenditure showed a strong correlation with positive family history to TD2 in young subjects (21-23), and our experience suggests that familiarity induces a precocious increase in body weight for visceral deposit of body fat (21, 24-26), maybe for a reduction in basal metabolism. Further analysis also showed that subjects with diagnosis to diabetes have a lower energy expenditure level compared to subjects with negative diagnosis to this illness (22, 27, 28). Regular physical activity reduces body weight in these subjects, confirming the protective role of sport on people's health (4, 29-31).
The aim of this study was to verify if in young healthy sedentary male and female there is positive correlation between family history to TD2 and an increase in body weight and fat mass, or alterations in basal glycaemia values. Moreover, according to our recent study (Bianco et al, 2013) (26), on that case we want to better understand how the degree (first or second) of family history may affect all measured parameters.

Materials and Methods

A cross-sectional study with a cohort of young adult people was performed by the University of Palermo in collaboration with the University of Padua. A number of 420 healthy sedentary subjects (183 male and 237 female) living in Palermo area were selected in 2012. All of them were Caucasians, with a middle-low socioeconomic status; the predominant diet regimen Sicily is the Mediterranean diet. These were then divided into three groups according on family history to diabetes type 2. First group (FH+) included all those who had a parent or first degree relative with type 2 diabetes (35 male and 44 female), second group (FH++) included all those subjects having second degree relatives with type 2 diabetes (32 male and 58 female) and third group (FH-) included those subjects with no family history to the illness; in this case we used FH- as control group. A proper six pages questionnaire was made up following the standards of the "MEDEOR clinics for metabolic disorders". It contained three main sections: a) Demographic information, number of hours of physical activity (hours/week), diet regimen and anthropometrics characteristics; b) History of illness; c) Family history to type 2 diabetes mellitus. Afterwards, the questionnaire was administered to the volunteers in order to detect family history to type 2 diabetes mellitus (TD2) and previous cardiovascular diseases such as myocardial infarction, stroke, vascular peripheral disease, hospitalisation for coronary heart disease (32).

Exclusion criteria

All those subjects resulting positive for the diseases above mentioned were excluded from the study. Moreover, we excluded from the study all people practicing more than 1 hour of physical activity per week and all people who declared were following intensive hypo-caloric diet regimen (a number of 22 subjects were excluded from the study). Height (Seca 709 ± 1g approximation, Hamburg – Germany), weight (Seca 220 ± 1mm approximation, Hamburg – Germany), shoulder, waist and hip circumferences (inelastic flexible meter with ± 1 mm approximation) were recorded. Body Mass Index (BMI, kg/m^2), Waist-Hip Ratio (WHR), Body Surface Area (BSA, m^2) were then calculated for each subject (33, 34). A bioelectrical impedance analysis (4 ways, 50 kHz frequency and 800 μA amplitude, Skylark, model BT-905 Taiwan, Korea) was then set for both male and female of all groups to assess Fat mass (FM) and Free Fat Mass (FFM) expressed both in kilograms (kg) and percentage (%). Fasting plasma glucose was finally measured for each subject with photometer Accu-chek Active (Roche Diagnostic, Germany), with a range measure of 10-600 mg/dl (0.6-33.3 mmol/L). A bioelectrical impedance analysis was performed following standardised procedures: participants have not exercised or taken a sauna within 7 hours before the test; participants were not allowed to drink alcohol (12 hours prior to

test); participants were not allowed to eat (4 hours prior to test); participants were not allowed to drink water (1 hour prior to test) participants did not have to be covered in sweat or soaked in urine (35). In order to evaluate body size (Shoulder Circum.), BSA and WHR we collected anthropometric measures. To evaluate body composition, for optimal accuracy and reliability we performed the BIA instead to use predictive equations.

Glucose levels were recorded through chemical reaction (mediator glucose-dehydrogenase pirrolochinolinechinone, GDH-PQQ), inducing colour translation on reactive zone. Ethical approval was established by the University of Palermo Ethics Committee (Commissione Etica del Dipartimento DISMOT) in Italy. The principles of the Italian data protection act (196/2003) were observed. All participants provided informed consent. The study was performed in compliance with the Helsinki Declaration.

Statistical Analysis

All recorded data were stored in excel format and were correlated when appropriate. The two-way ANOVA analysis of variance with Bonferroni post tests was used for statistical considerations through Instat-GRAPHPAD PRI-SM 5 Software (San Diego, USA).*P* values were considered significant when <0.05.

Results

The FH+ males (Table 1) had a greater body mass index ($P<0.01$) with significant increase of waist and hip circumferences and consequently in WHR ($P<0.01$) than other groups. Table 2 shows that older FH+ females have an increase in body weight ($P<0.01$), body surface area ($P<0.005$), waist ($P<0.005$) and hip circumferences ($P<0.05$), greater than other groups. As showed in Table 3 and 4, FH+ subjects had an increase in FM, in relative ($P<0.05$ between males, $P<0.005$ between females) and absolute values ($P<0.01$ between males, $P<0.005$ between females), with worse FFM/FM ratio ($P<0.01$ between males, $P<0.05$ between females) compared to FH++ and the control group (FH-). Table 5 and 6 show blood glucose levels, of male and female subgroups, related to body parameters. Only FH+ males had a significant reduction in fasting glucose levels for kg FM unit ($P<0.01$). FH+ women showed lower levels of fasting glucose levels for kg of BW and FM unit ($P<0.005$) and for kg of BSA ($P<0.01$). Figure 1 shows the linear trend between the basal blood fasting glucose levels and body fat mass ($r = 0.12$; $r^2 = 0.014$). Figure 2 and 3 are highlighting the results stratified by gender.

Table 1: Anthropometric parameters of male subjects

Variable	FH+ (n = 35)	FH++ (n = 32)	FH- (n = 116)	*p*
Age, years	34.80 ± 12.03	25.50 ± 6.39	28.20 ± 10.41	0.0005
Height, cm	172.77 ± 6.57	174.27 ± 8.89	174.02 ± 6.33	NS
Body weight, kg	82.96 ± 18.51	75.63 ± 12.71	77.78 ± 11.58	NS
BMI, kg/m^2	27.72 ± 5.62	24.83 ± 3.20	25.67 ± 3.58	0.0078
BSA, m^2	1.96 ± 0.21	1.90 ± 0.19	1.92 ± 0.15	NS
Shoulder circumference, cm	113.73 ± 8.53	111.73 ± 9.91	114.00 ± 9.23	NS
Waist circumferences. cm	94.21 ± 15.47	84.17 ± 10.54	86.93 ± 10.47	0.0007
Hip circumferences. cm	95.21 ± 13.42	87.34 ± 9.10	89.44 ± 9.34	0.0360
WHR	0.99 ± 0.05	0.96 ± 0.03	0.97 ± 0.04	0.0079

NS: no significance

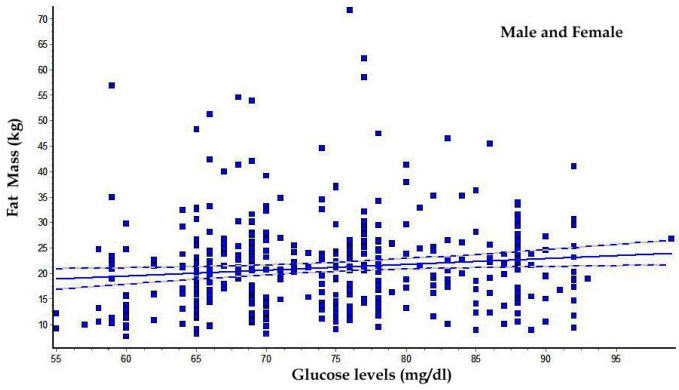

Fig. 1: Linear trend between glucose levels and fat mass (kg); (correlation Coefficient r = 0.1199; r2 = 0.01437)

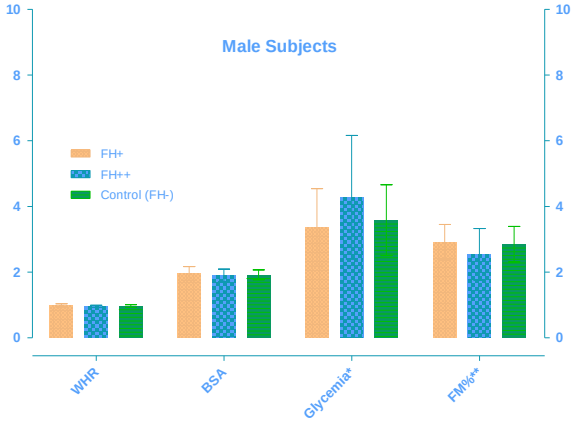

Fig. 2: Male Subjects variables: WHR (Waist–hip ratio); BSA (Body Surface Area, m^2); Glycemia (* Glucose levels reported in mg/dl ·kg FM^{-1}); FM% (** Body Fat Mass reported in % divided by 10)

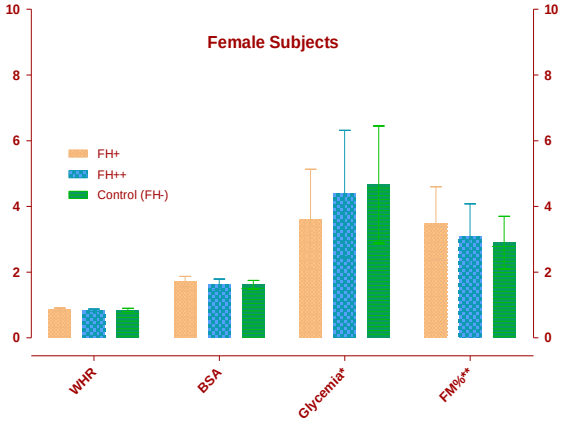

Fig. 3: Female Subjects variables: WHR (Waist–hip ratio); BSA (Body Surface Area, m^2); Glycemia (* Glucose levels reported in mg/dl ·kg FM^{-1}); FM% (** Body Fat Mass reported in % divided by 10)

Table 2: Anthropometric parameters of female subjects

Variables	FH+ (n = 44)	FH++ (n = 58)	FH- (n = 135)	*p*
Age, years	34.25 ± 12.31	27.62 ± 9.23	32.73 ± 11.71	0.0047
Height, cm	162.28 ± 6.27	160.18 ± 6.57	159.24 ± 5.09	NS
Body weight, kg	67.58 ± 14.67	61.51 ± 12.82	60.75 ± 10.89	0.0052
BMI, kg/m^2	25.77 ± 5.85	23.98 ± 4.85	23.96 ± 4.14	NS
BSA, m^2	1.71 ± 0.16	1.63 ± 0.16	1.62 ± 0.13	0.0015
Shoulder circumferences, cm	100.84 ± 8.87	98.02 ± 7.05	98.38 ± 6.00	NS
Waist circumferences, cm	82.82 ± 12.53	75.75 ± 10.79	77.46 ± 10.47	0.0040
Hip circumferences. cm	96.07 ± 13.57	90.55 ± 12.63	90.72 ± 11.35	0.0296
WHR	0.86 ± 0.05	0.84 ± 0.04	0.85 ± 0.05	NS

NS: no significance

Table 3: Body composition (BIA) of male subjects

Variables	FH+ (n = 35)	FH++ (n = 32)	FH- (n = 116)	*P*
H_2O, litres	39.06 ± 8.26	37.60 ± 7.50	36.95 ± 5.57	NS
FM, %	29.10 ± 5.41	25.46 ± 7.97	28.59 ± 5.43	0.0191
FFM, %	70.90 ± 5.41	74.54 ± 7.97	71.41 ± 5.43	0.0191
FM, kg	24.37 ± 7.83	19.23 ± 6.87	22.35 ± 5.85	0.0052
FFM, kg	58.59 ± 12.40	56.40 ± 11.25	55.43 ± 8.36	NS
FFM/FM	2.63 ± 1.10	3.51 ± 1.94	2.72 ± 1.20	0.0085

NS: no significance

Table 4: Body composition (BIA) of female subjects

Variables	FH+ (n = 44)	FH++ (n = 58)	FH- (n = 135)	*P*
H_2O, litres	28.33 ± 3.48	27.33 ± 3.20	27.96 ± 3.31	NS
FM, %	35.28 ± 11.12	31.76 ± 9.82	29.90 ± 8.32	0.0039
FFM, %	64.72 ± 11.12	68.24 ± 9.82	70.10 ± 8.32	0.0039
FM, kg	25.08 ± 13.86	20.51 ± 11.19	18.81 ± 8.49	0.0026
FFM, kg	42.50 ± 5.22	40.99 ± 4.80	41.94 ± 4.97	NS
FFM/FM	2.09 ± 0.90	2.43 ± 1.00	2.60 ± 0.97	0.0102

NS: no significance

Table 5: Fasting blood glucose levels of male subject in absolute and relative values

Glucose levels	FH+ (n = 35)	FH++ (n = 32)	FH- (n = 116)	*P*
mg/dl	73.86 ± 10.14	71.72 ± 9.81	74.30 ± 9.31	NS
mg/dl · kg BW^{-1}	0.93 ± 0.24	0.97 ± 0.20	0.97 ± 0.18	NS
mg/dl · kg FFM^{-1}	1.32 ± 0.36	1.33 ± 0.34	1.37 ± 0.29	NS
mg/dl · kg FM^{-1}	3.36 ± 1.18	4.28 ± 1.88	3.58 ± 1.08	0.0076
mg/dl · kg BSA^{-1}	38.15 ± 6.81	38.15 ± 6.60	38.91 ± 5.59	NS

NS: no significance

Table 6: Fasting blood glucose levels of female subject in absolute and relative values

Glucose levels	FH+ (n = 44)	FH++ (n = 58)	FH- (n = 135)	*P*
mg/dl	73.61 ± 8.93	73.09 ± 8.75	75.33 ± 9.29	*NS*
mg/dl · kg BW^{-1}	1.13 ± 0.23	1.24 ± 0.28	1.27 ± 0.23	0.0046
mg/dl · kg FFM^{-1}	1.75 ± 0.29	1.81 ± 0.32	1.82 ± 0.29	NS
mg/dl · kg FM^{-1}	3.61 ± 1.52	4.39 ± 1.93	4.67 ± 1.78	0.0031
mg/dl · kg BSA^{-1}	43.25 ± 6.40	45.22 ± 7.32	46.75 ± 6.30	0.0081

NS: no significance

Discussion

The development of TD2 during years has relevantly increased in occidental countries as shown by WHO (32, 36-38). This has demonstrated the multifactorial pathogenesis of this disease correlating its manifestation not only with genetic factors or predispositions but also with age, gender,

un-healthy life styles, obesity and physical inactivity (10, 34, 39, 40). Our results are confirming the hypotheses that there are few anthropometrics and physiological variables strongly related to family history, predominantly linked to a first degree of familiarity. In addition, environmental factors are determinant for the pathogenesis of the illness (41, 42). This great variability of risk factors leads to a multiple therapeutic control: new drugs are now used to control this disease, such as incretins Gip (gastric polypeptide inhibitor) and Glp-1 (glucagone similar peptide) or similar drugs likesitagliptine and exenatide. Some studies have showed that TD2 patients produce lower levels of incretines, which normally promote insulin synthesis and release after food intake (43-48).Knowing phenotype, metabolic or blood parameters in subjects with positive family history to diabetes may prevent the development of this disease. It has been also shown that FH to TD2 can lead to unbalanced energy expenditure, so consequently may influence the body composition (21, 22, 24, 25). The present study are confirming what found in scientific literature and are showing, in addiction, that in subjects with first degree of FH there is an increase of body weight for an augment of body fat (this body composition modification may determine an alterations of energy expenditure) (22, 26, 28, 49). It is also confirmed that in sedentary man and women there is a strong correlation between FH TD2 and precocious increase in body weight (22, 50, 51).

These increases involve body fat mass, especially in FH+. Moreover when the same values are related to phenotype parameters a strong linear correlation with FM, in both sexes was shown even though, the results are more evident in women, maybe for the inter-generative transmission of illness predisposition (3-9, 51).

It is hypothesized that the muscle cells of these subjects undergo early alterations (genetically determined) in insulin-independent glucose transport, which could augment glucose uptake through insulin-dependent pathways, with the risk of hyper-insulinemia and peripheral insulin resistance (11). The most evident, direct factor contributing to such alterations could be a family history of diabetes, related to unknown factors thought to be linked to genes encoding altered poorly functioning proteins, inducing increase in body weight (hypertrophic effect of insulin) and particularly of body fat mass (lipogenic effect of insulin)(52-54). Coming up, the insulin-dependent compensatory mechanisms could deteriorate and break down, resulting in a clinical manifestation of the disease. In FH+, regular physical activity reduces the increase in glucose uptake through insulin-dependent pathways, stimulating the alternative, although defective, function of insulin-independent mechanisms, thus improving glucose control and reducing body mass, in particular body fat mass (55). The deficient insulin-dependent mechanisms could acts as a brake, impairing metabolic response and subsequent oxygen consumption during regular physical activity, which has also been demonstrated in studies conducted in normal conditions (22, 24).

Conclusion

Family history on TD2 especially in FH+ influences body composition and weight in healthy sedentary male and women. The multifactorial phatogenetic mechanism of TD2 makes this disease difficult to approach but it is also known the protective role of regular physical activity in order to maintain health and control body weight and blood glycemia. FH+ compared to other groups showed greater body mass and WHR. This important finding, highlighted for the first time on that study, is confirming the hypothesis that the first degree of FH is a strong indicator of precocious modifications of body composition.

Other studies are needed to confirm these encouraging results especially for unhealthy or athletes with family history to TD2.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

Acknowledgements

The study was supported by the MEDEOR Research Institute – Palermo, with the grant code AED-SELINO-S6/2011-2012. We are grateful to all participants for their contributions. The authors declare that there is no conflict of interests.

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