FAMILY HISTORY OF TYPE 2 DIABETES IS ASSOCIATED WITH METABOLIC SYNDROME IN OBESE FEMALE SUBJECTS

HISTÓRIA FAMILIAR DE DIABETES TIPO 2 ESTÁ ASSOCIADA COM SÍNDROME METABÓLICA EM INDIVÍDUOS OBESOS DO SEXO FEMININO

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ABSTRACT

The aim of this study was to evaluate the association between the family history (FH) of type 2 diabetes and metabolic syndrome (MetS) in a group of non-diabetic obese female subjects. A cross-sectional study was conducted in 239 female patients with obesity, regularly attending the Internal Medicine Division's outpatient clinic (Hospital de Clínicas de Porto Alegre, Brazil). The inclusion criteria were patients with body mass index ≥30 kg/m^2 and absence of type 2 diabetes. The FH was considered positive if a first degree relative had a diagnosis of diabetes. Seventy-four of 239 patients evaluated (30%) had a positive FH for type 2 diabetes. Patients with positive FH had higher waist/hip ratio and MetS more often than patients with negative FH. FH of type 2 diabetes was associated with MetS in this sample of non-diabetic obese female patients. Waist/hip ratio and fasting plasma glucose, markers of insulin resistance, were also associated with FH of type 2 diabetes. The simple question: "Do you have a FH of type 2 diabetes?" may help to identify the obese patients that should be better evaluated and intensively treated with the objective of preventing type 2 diabetes.

Keywords**:** *Obesity; family history; type 2 diabetes; metabolic syndrome*.

RESUMO

O objetivo deste estudo foi avaliar a associação entre história familiar (HF) de diabetes melito tipo 2 (DM2) e síndrome metabólica (SM) em um grupo de mulheres obesas não-diabéticas. Conduzimos um estudo transversal com 239 mulheres com obesidade, regularmente atendidas no ambulatório de medicina interrna do Hospital de Clínicas de Porto Alegre, Brasil. Os critérios de inclusão foram pacientes com índice de massa corporal ≥30 kg/m^2 e ausência de DM2. A HF de DM2 foi considerada positiva se um familiar de primeiro grau tivesse o diagnóstico de diabetes. Setenta e quatro das 239 pacientes avaliadas (30%) tiveram uma HF positiva de DM2. Pacientes com HF positiva tiveram maior razão cintura/quadril e mais frequentemente a presença de SM que as pacientes com HF negativa. A HF de DM2 foi associada com SM nesta amostra de pacientes femininas obesas não-diabéticas. A razão cintura/quadril e a glicemia de jejum, ambos marcadores de resistência à ação da insulina, foram também associadas com HF de DM2. A simples pergunta: "Você tem uma HF de DM2"? pode ajudar a identificar pacientes obesos que devem ser mais bem avaliados e intensamente tratados com o objetivo de prevenção do DM2.

Unitermos: *Obesidade, síndrome metabólica, história familiar, diabetes melito tpo 2.*

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The recent epidemic of obesity has been accompanied by an increased incidence of type 2 diabetes (1). In Brazil, obesity and overweight are present in 9.7 and 28.3% of the adults, respectively (2). The higher frequency is seen among women, affecting 50% of women between 50 and 69 years old (2). Obesity and family history (FH) of type 2 diabetes are important predictors of type 2 diabetes (3). Subjects with FH of type 2 diabetes are more insulin resistant and/or have decreased insulin secretion compared to those without FH of diabetes (4). FH of type 2 diabetes is also associated with metabolic syndrome (MetS), abdominal obesity and hyperglycemia (5). MetS is an important cluster of cardiovascular disease (CVD) risk factors that contribute to insulin resistance.

The aim of this report was to evaluate the association between the FH of type 2 diabetes and MetS in a group of non-diabetic obese female subjects.

METHODS

A cross-sectional study was conducted in 239 female patients with obesity, regularly attending the Occupational Medicine Division's outpatient clinic at Hospital de Clínicas de Porto Alegre. The inclusion criteria were patients with body mass index (BMI) ≥30 kg/m^2, absence of type 2 diabetes [established by clinical history, normal fasting glycemia (≤125 mg/dl)

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and a 2-h oral glucose tolerance test with 75 g glucose < 200 mg/dl] (6). The FH was considered positive if a first degree relative had a diagnosis of diabetes. The Ethics Committee of the hospital approved the project, and written informed consent was obtained from all patients.

Patients underwent an interview and clinical examination to record demographic and anthropometric data. Blood pressure evaluations were performed with the patients in regular use of their medications (including antihypertensive medications). The mean of two office blood pressure measurements (left arm and with the patient in a sitting position, after a 10-min rest) were considered for the analysis.

The presence of MetS was determined according to 3 criteria. The World Health Organization (WHO) criterion requires the presence of two or more of the following, besides diabetes: hypertension (blood pressure ≥140/90 mm Hg and/or antihypertensive treatment), triglycerides ≥150 mg/dl, HDL <35 mg/dl in men and <39 mg/dl in women, obesity (body mass index >30 kg/m^2 and/or waist-hip ratio >0.90 in males and >0.85 in females), presence of albuminuria (micro or macroalbuminuria) (7). National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), as modified by the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (8), requires that the patients have three or more: waist circumference ≥102 cm in men and ≥88 cm in women, triglycerides ≥150 mg/dl, HDL <40 mg/dl in men and <50 mg/dl in women, blood pressure ≥135/85 mm Hg or use of antihypertensive drugs and fasting glucose ≥100 mg/dl. International Diabetes Federation (IDF) requires that the patients have waist circumference >94 cm for men and >80 cm for women and two or more of the following were present: triglyceride level ≥150 mg/dl, HDL cholesterol <40 mg/dl if men or <50 mg/dl if women, blood pressure >130/85 mm Hg or taking antihypertensive medication, and fasting glucose >100 mg/dl (9).

Plasma glucose was measured by the glucose-peroxidase colorimetric enzymatic method (Biodiagnostica). Creatinine was measured by the Jaffé method and the lipid profile by colorimetric methods. The glomerular filtration rate (GFR) was estimated using the formula of the Modification of Diet in Renal Disease Study (10): 186 x [serum creatinine $^{-1.154}$ x age$^{-0.203}$ x (0.742, if female) x (1.210, if of African descendant)].

Student's T test was used for continuous variables and the χ^2 test was used for categorical variables. Data were expressed as mean ± S.D., except for triglycerides, that were log-transformed for analysis and expressed as median and range. A P <0.05 was considered to be significant.

RESULTS

Seventy-four of 239 patients evaluated (30%) had a positive FH for type 2 diabetes. Clinical and laboratory data according to the presence or absence of diabetes FH are described in Table 1. Patients with positive FH had a higher waist/hip ratio and MetS more often than patients with negative FH. There were no differences regarding age, BMI, blood pressure levels, and ethnic distribution between groups. Regarding laboratory values, the only difference found was higher fasting plasma glucose among those with positive FH compared to those with negative FH. The lipid profile as well as the GFR were not different between patients with and without diabetes FH.

Table 1: Descriptive data for patients with and without family history of type 2 diabetes.

	Family History of Diabetes		
	Positive N (74)	Negative N (165)	P
Age (years)	39.8 ± 7.2	39.2 ± 8.7	0.590
Ethnicity (white) n (%)	41 (55.4)	111 (67.5)	0.080
BMI (kg/m^2)	34.4 ± 3.5	35.0 ± 3.8	0.240
Waist circumference (cm)	102 ± 9	100 ± 9	0.10
Systolic blood pressure (mmHg)	126.1 ± 17	122.7 ± 13	0.11
Diastolic blood pressure (mmHg)	80.6 ± 10	79.6 ± 9.7	0.49
Hypertension n (%)	25 (33.8)	44 (27)	0.29
Total cholesterol (mg/dl)	198 ± 42	193 ± 38	0.43
HDL cholesterol (mg/dl)	51 ± 12	53 ± 13	0.39
LDL cholesterol (mg/dl)	121 ± 35	117 ± 33	0.47
Triglycerides (mg/dl)	177 (67-521)	97 (43–303)	0.07
Fasting glucose (mg/dl)	97 ± 9	93 ± 9	0.04
GFR (ml/min per 1.73m^2)	95 ± 17	95 ± 30	0.89
MetS WHO n (%)	25 (34)	32 (19.6)	0.03
MetS NCEP n (%)	32 (44)	41 (24.7)	0.006
MetS IDF n (%)	34 (45.8)	44 (27)	0.009

Data are means ± SD, median (range) or %. BMI= body mass index, GFR= glomerular filtration rate, WHO= World Health Organization, NCEP= National Cholesterol Education Program, IDF= International Diabetes Federation, MetS= metabolic syndrome.

DISCUSSION

FH of type 2 diabetes was associated with MetS in this sample of non-diabetic obese female patients, independently of the definition used. Waist/hip ratio and fasting plasma glucose, both markers of insulin resistance, were also associated with FH of type 2 diabetes.

The association between FH and risk for diabetes has been previously demonstrated (11,12). The presence of MetS has been considered a risk factor for CVD and early mortality in non diabetic subjects (13,14). MetS is also an important risk factor for developing type 2 diabetes and is present in more than 80% of these patients (15). Patients with diabetes and MetS are at greater risk, not only for macrovascular disease but also for microvascular complications (15).

All subjects included in the present study were obese. Obesity is a well known risk factor for CVD, diabetes and MetS. Probably for this reason, there was a high prevalence of FH of diabetes (30%).

This is the first report showing the association between FH of type 2 diabetes and MetS in Brazilian obese women. A possible limitation of the present study is the use of self-report for parental diabetes status. This is prone to bias due to unknown diabetes among parents. Even with this potential underreport, positive FH of diabetes was associated with MetS.

Recently, a study in the American population confirmed the FH of diabetes is independently associated with diabetes and suggests the possibility of adding FH to public health strategies to detect and prevent diabetes (16). This idea is very interesting, especially in developing countries. FH is easy to obtain and conveniently conveys information on genes and environment shared by close relatives (17). The cost-effectiveness of adding FH to the health programs of patients with obesity needs be evaluated. The simple question: "Do you have a FH of type 2 diabetes?" may help to identify the obese patients that should be better evaluated and intensively treated for the purpose of preventing type 2 diabetes.

The association between MetS and positive FH of diabetes in obese patients probably increases or anticipates the risk for diabetes and CVD, but this still needs to be evaluated and proved. Therefore, so far, the presence of FH of diabetes in obese patients should be evaluated independently of presence of MetS.

In summary, obese women with positive FH for diabetes more frequently have MetS. The simple inclusion and valorization of this information in the routine evaluation of obese subjects might help decrease the burden of diabetes and its consequences.

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