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Metabolic syndrome at follow-up in women with and without gestational diabetes mellitus in index pregnancy

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Abstract

We prospectively studied 262 women with prior gestational diabetes mellitus (GDM) and 66 control women to compare their prevalence of metabolic syndrome and its relationship with insulin secretion and sensitivity. A 75-g oral glucose tolerance test was scheduled 5 years after delivery along with lipid profile, anthropometrics, and blood pressure measurement. Metabolic syndrome was defined according to the National Cholesterol Education Program 2001, and insulin sensitivity and secretion were estimated with the homeostasis model assessment. Women with prior GDM had similar insulin sensitivity and lower insulin secretion than control women. In comparison with control women, women with prior GDM had higher blood pressure, waist circumference, very low-density lipoprotein cholesterol, and oral glucose tolerance test blood glucose values but, with the exception of fasting hyperglycemia, did not have an increased prevalence of metabolic syndrome or its components. The multivariate prediction of metabolic syndrome and its components was similar with age and current homeostasis model assessment–insulin secretion and resistance indexes or with age, obesity, and GDM. The main predictor was current insulin resistance in the first case and obesity in the second, obesity being the best predictor overall. We conclude that in our population and at midterm follow-up, women with prior GDM have a decreased insulin secretion and display a higher prevalence of fasting hyperglycemia but not the full-blown picture of metabolic syndrome. Obesity, a surrogate index of insulin resistance, is the best predictor of metabolic syndrome at follow-up.
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1. Introduction

Women with prior gestational diabetes mellitus (GDM) have an increased risk of later diabetes mellitus (DM), abnormal glucose tolerance [1-3], and cardiovascular risk factors and events [1,2,4-8]. In some studies, the increased prevalence of cardiovascular risk factors is only evident in women with DM or abnormal glucose tolerance at follow-up [2,3,9]. After delivery, these women show defects in insulin action and secretion even when glucose tolerance is normal [5,10-13]. In turn, insulin resistance has been related to cardiovascular disease and may play a pathogenic role in the development of cardiovascular risk factors [14,15]. Therefore, in these women, the link between the various cardiovascular risk factors could be an increased insulin resistance. Furthermore, an improvement in lipid profile has been described in patients with type 2 diabetes when glycemic control is ameliorated with insulin therapy [16], indicating that the expression of metabolic syndrome can be influenced by insulin availability.

The aim of this study was to evaluate the prevalence of metabolic syndrome and its components (National Cholesterol Education Program [NCEP] 2001 criteria) in women with previous GDM and control women at 5 to 10 years follow-up, and to analyze the relationship between prevalence and insulin resistance and secretion. To date, only 2 papers in the literature have described the prevalence of metabolic syndrome according to the NCEP 2001 criteria in women with GDM [8,17].

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2. Patients and methods

2.1. Description of patients and protocol

Nine hundred eighty-two women, who were diagnosed of GDM between 1986 and 1993 and attended at the Diabetes and Pregnancy Unit at the Hospital de Sant Pau in Barcelona, were invited to participate in this prospective study, and 262 took part in it. Diagnostic and treatment protocols during pregnancy have been described in Ref [18]. All women with GDM were advised to return 6 weeks after delivery or cessation of breast-feeding and at 5-year intervals for metabolic testing. Information about risk of later diabetes and lifestyle recommendations (importance of low-fat diet, weight reduction, exercise, and no smoking) were given to all women during pregnancy, 3 to 5 days postpartum, and at each postpartum evaluation. The present study was initiated at the 5-year follow-up. The 66 control women who participated in the study had a pregnancy in the same period and a normal screening or oral glucose tolerance test (OGTT) at a gestational age of 32 weeks or more.

The study protocol included the following:

1. History taking about clinical variables before, during, and after index pregnancy. Before pregnancy, we recorded age, body mass index (BMI), previous pregnancies, history of poor obstetric outcome and abnormal glucose tolerance, nondiagnostic hyperglycemia, or GDM (before index pregnancy). During pregnancy, data collected included oral glucose challenge/OGTTs, hemoglobin A_{1c}, preterm birth, and macrosomia. After pregnancy, we recorded family history of DM, additional pregnancies and GDM, diagnosis of DM, hypertension or dyslipidemia, and current drug therapy. Additional variables (ie, prepregnancy family history of DM and diabetes-related antibodies in the study group) were only used to test the validity of the groups.
2. Physical examination included height, weight, blood pressure, and waist circumference (measured horizontally at the level of the narrowest part of the torso in the standing position).
3. A standard 75-g glucose OGTT was performed after eating a 8368-kJ (2000-kcal) diet ($\geq$150 g carbohydrates) for 3 days.
4. Fasting lipid profile included total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C).
5. The beta-cell function and insulin sensitivity were estimated in a subgroup of 135 women with previous GDM and 65 control women with the homeostasis model assessment (HOMA) indices (mathematical estimation, single fasting sample of insulin and plasma glucose) [19]. The beta-cell function was expressed as the percentage of insulin secretion in relation to a group of healthy women younger than 35 years and without diabetes in first-degree relatives [20] and insulin resistance as a HOMA index higher than the 90th centile of this group. Insulin sensitivity was defined as the reverse of HOMA index. The disposition index was calculated as the product between insulin secretion and sensitivity. Metabolic syndrome and its components were defined according to the NCEP 2001 criteria [21].

2.2. Blood tests

Blood samples were obtained after an overnight fast (12 hours) and 30, 60, and 120 minutes after 75-g oral glucose administration. A glucose oxidase method adapted to an automatic autoanalyzer was used to measure glucose concentrations in plasma. Serum insulin concentrations were measured with an immunoradiometric assay (Biosource Europe, Nivelles, Belgium) without cross-reactivity with proinsulin. Interassay coefficient of variation were 12.2% and 4.7% at concentrations of 70 and 259 pmol/L.

Table 1
Clinical characteristics and biochemical tests in index pregnancy in control women and women with previous GDM

	Control women (n = 66)	Women with GDM (n = 262)
Age (y)	29.6 ± 4.9	32.1 ± 4.3*
Prior abnormal glucose tolerance[a] (%)	1.5	3.4
Previous pregnancies (%)	28.6	68.8*
History of poor obstetric outcome (%)	0	12.8*
Pregestational BMI (kg/m^2)	21.8 (17.6-27.5)	23.1 (17.8-36.3)*
Blood glucose in 50-g glucose challenge at a gestational age $\geq$32 wk (mmol/L)	7.2 ± 1.1	–
Gestational age at diagnosis (wk)	–	31 (9-40)
Diagnostic OGTT (100-g glucose)		
Blood glucose 0 min (mmol/L)	–	4.9 (3.1-7.0)
Blood glucose 60 min (mmol/L)	–	11.7 (8.1-15.5)
Blood glucose 120 min (mmol/L)	–	10.2 (7.1-15.8)
Blood glucose 180 min (mmol/L)	–	7.4 (3.4-11.9)
AUC	–	28.0 (24.0-34.9)
No. of abnormal values	–	2 (2-4)
Glycated hemoglobin after diagnosis (SD)	–	−1.16 (−4.29 to 3.66)
Insulin therapy (%)	–	62
Antibody positivity (%) (islet cell/GAD/ tyrosine phosphatase)	–	11.1
Preterm birth	1.8	3.0
Macrosomia	7.4	2.6

GAD indicates glutamic acid decarboxylase.

[a] Prior abnormal glucose tolerance: impaired glucose tolerance, abnormal glycemia (nondiagnostic hyperglycemia), or GDM before index pregnancy.

* $P < .05$.

Glycated hemoglobin after GDM diagnosis was expressed in SDs around the mean.

All lipid measurements were performed in plasma-EDTA samples. Total cholesterol and triglycerides were assayed by fully enzymatic methods in a Hitachi 911 analyzer (Roche Diagnostics, Basel, Switzerland). High-density lipoprotein cholesterol was measured by means of a direct method, without precipitation, using α-cyclodextrin sulfate, $MgCl_2$, and polyethylene glycol–pretreated cholesterol esterase and oxidase to specifically measure HDL-C (Roche Diagnostics). Low-density lipoprotein cholesterol and VLDL-C were measured by an ultracentrifugation-based method after separation of VLDL-C (density [d] <1.006 kg/L) and measurement of HDL-C content of the d >1.006 kg/L fraction. Non–HDL-C was calculated as the difference between total and HDL-C.

2.3. Statistical analyses

Statistical analysis was conducted using SPSS 10.0 statistical software (SPSS, Chicago, Ill). Logarithmic transformation was performed for non–HDL-C and triglycerides. Quantitative variables are expressed as mean (SD) or median (range) according to their distribution (normal or non-normal). Bivariate analysis was performed using χ^2 test to compare categorical variables and Student *t* and Mann-Whitney *U* tests for continuous variables according to their distribution. Multiple logistic regression was used for multivariate analysis with the following strategy:

- To assess the validity of the study group, a logistic regression analysis was performed with attendance at follow-up as the dependent variable and as potential predictors: prepregnancy characteristics (family history of DM, previous pregnancies and abnormal glucose tolerance, history of poor obstetric outcome, and BMI) and index pregnancy characteristics (maternal age and gestational age at diagnosis, diagnostic OGTT, glycated hemoglobin A_{1c} after diagnosis, insulin therapy, antibody positivity for islet cell, glutamic acid decarboxilase or tyrosine phosphatase antibodies, preterm birth, and macrosomia). To assess the validity of the control group, a logistic regression analysis was performed with participation in the follow-up study as the dependent variable and maternal age at pregnancy, prepregnancy BMI, blood glucose response to 50-g glucose challenge, and macrosomia as potential predictors.
- To compare GDM and control women participating in the study, first, the following variables were analyzed in a bivariate analysis: background (family history of DM, additional pregnancies, and GDM), characteristics in index pregnancy (maternal age, prior abnormal glucose tolerance, previous pregnancies, history of poor obstetric outcome, pregestational BMI, preterm birth, and macrosomia), characteristics at follow-up (age, BMI, systolic and diastolic blood pressure, waist circumference, and length of follow-up), and blood tests at follow-up (OGTT blood glucose, total cholesterol, triglycerides, HDL-C, non–HDL-C, LDL-C, and VLDL-C). Second, a multivariate analysis was performed using GDM or control condition as the dependent variable and metabolic syndrome and its components as potential markers.
- Metabolic syndrome and its components in relation to prior GDM and insulin resistance and secretion. First, the presence of metabolic syndrome and its components was compared in GDM and control women before and after splitting the groups according to either insulin resistance or obesity. Second, logistic regression analyses were performed with metabolic syndrome and its components as dependent variables and different sets of predictors: (*a*) age, control group/prior GDM, insulin secretion, and resistance; and (*b*) age, control group/prior GDM, and obesity.
- A *P* value of .05 was considered significant.

3. Results

3.1. Validity of the groups

Women with prior GDM who came to follow-up were older (odds ratio [OR] 1.05, 95% confidence interval [CI]

Table 2
Clinical characteristics and biochemical tests at follow-up in control women and women with previous GDM

	Control women	Women with GDM
Family history of diabetes mellitus (%)	43.9	50.8
Additional pregnancies (%)	22.7	20.1
Additional GDM if pregnancy (%)	6.6	51.9*
Age at follow-up (y)	39.1 ± 5.5	40.6 ± 4.8
BMI (kg/m^2)	24.4 (18.3-38.4)	24.8 (17.9-40.2)
Systolic blood pressure (mm Hg)	110 (80-140)	120 (85-180)*
Diastolic blood pressure (mm Hg)	70 (50-100)	78 (50-100)*
Waist circumference (cm)	72.5 (59-108)	76 (59-118)*
Length of follow-up (y)	7.3 (3.5-13.3)	7.2 (5.3-13.1)
OGTT at follow-up (75-g glucose)		
Blood glucose 0 min (mmol/L)	4.8 (3.8-6)	5.0 (4.2-7.4)*
Blood glucose 30 min (mmol/L)	7.4 (4.2-10.0)	9 (5.6-14.1)*
Blood glucose 60 min (mmol/L)	6.5 ± 2	9.1 ± 2.5*
Blood glucose 120 min (mmol/L)	4.9 (2.3-8.5)	6.2 (3.6-14.0)*
AUC	18.4 (10.7-27.8)	23.4 (15.6-39.8)*
Total cholesterol (mmol/L)	5.1 (3.7-7.0)	5.2 (3.8-8.2)
Non–HDL-C (mmol/L)	3.5 (1.9-8.5)	3.7 (2-7)
Tryglicerides (mmol/L)	0.69 (0.33-2.17)	0.85 (0.4-4.0)
HDL-C (mmol/L)	1.5 (0.8-2.2)	1.4 (0.8-2.6)
LDL-C (mmol/L)	3.2 (2.2-5.3)	3.4 (2.1-6.4)
VLDL-C (mmol/L)	0.18 (0.02-0.86)	0.35 (0.06-1.26)*

* $P < .05$.

Table 3
Prevalence of metabolic syndrome components (NCEP 2001 criteria) at follow-up in women with previous GDM and control women (%)

Variables	Control women (n = 66)	GDM women (n = 262)	*P*
Waist circumference >88 cm	9.1	19.1	ns
Triglycerides ≥1.7 mmol/L	6.1	5.3	ns
HDL-C <1.3 mmol/L	30.3	33.2	ns
Blood pressure ≥130/85 mm Hg	28.8	41.6	.066
Fasting glucose ≥6.1 mmol/L	0	6.5	.048
Metabolic syndrome (≥3 of the former)	6.1	11.1	ns

In multivariate logistic regression analysis with GDM or control group as the dependent variable and metabolic syndrome and its components as independent variables, the single predictive variable was fasting glucose at follow-up of ≥6.1 mmol/L (OR, 983; 95% CI, 0-2.9 × 10^{15}, *P* value of the model = .005).

1.02-1.09) had a lower prevalence of previous abnormal glucose tolerance (OR, 0.35; 95% CI, 0.15-0.84), and lower area under the curve (AUC) on the diagnostic OGTT (OR, 0.91; 95% CI, 0.85-0.97) than those without follow-up. Control women participating in the study had a higher blood glucose response to 50-g glucose challenge than the nonparticipating women who delivered in the center in the same period (OR, 1.396; 95% CI, 1.143-1.704).

3.2. Cardiovascular risk factors in GDM and control women

During pregnancy, women with previous GDM were older, had a higher pregestational BMI, and reported a higher prevalence of previous pregnancies and poor obstetric outcomes than control women (Table 1). At follow-up, women with previous GDM reported a higher rate of GDM diagnosis in later pregnancies and had a higher waist circumference, higher figures of systolic and diastolic blood pressure, higher blood glucose concentrations in the OGTT, and also higher levels of VLDL-C than control women (Table 2).

When metabolic syndrome components were considered according to the cut-off points of NCEP 2001, control women and those with former GDM differed only in the rate of fasting hyperglycemia whereas high blood pressure reached borderline significance (Table 3). Moreover, multivariate logistic regression analysis only identified fasting hyperglycemia (OR, 983; 95% CI, 0-2.9 × 10^{15}, *P* value of the model = .005) as an independent discriminator between prior GDM or control condition.

When both groups were categorized according to current obesity at follow-up (Table 4A), obese women, both from control and GDM groups, had a higher prevalence of

Table 4
Prevalence of metabolic syndrome components (NCEP 2001 criteria) at follow-up in women with previous GDM and control women (%) according to obesity or insulin resistance

A. According to the presence of obesity (BMI ≥30 kg/m^2) at follow-up

Variables	Control women		Women with GDM	
	BMI <30 kg/m^2 (n = 57)	BMI ≥30 kg/m^2 (n = 9)	BMI <30 kg/m^2 (n = 210)	BMI ≥30 kg/m^2 (n = 52)
Waist circumference >88 cm	1.8	55.6[a]	5.2	75[b]
Triglycerides ≥1.7 mmol/L	1.8	33.3[a]	2.4	17.3[b]
HDL-C <1.3 mmol/L	24.6	66.7[a]	28.1	57.7[b]
Blood pressure ≥130/85 mm Hg	23	67[a]	33.8	73.1[b]
Fasting glucose ≥6.1 mmol/L	0	0	3.3	19.2[b]
Metabolic syndrome (≥3 of the former)	1.8	33.3[a]	2.9	44.2[b]

B. According to the presence of insulin resistance (HOMA index ≥90th centile of the reference group)[c]

Variables	Control women		Women with GDM	
	Without IR (n = 54)	With IR (n = 11)	Without IR (n = 102)	With IR (n = 33)
Waist circumference >88 cm	3.7	36.4[d]	10.1	46.7[e]
Triglycerides ≥1.7 mmol/L	1.9	27.3[d]	2	15.2[e]
HDL-C <1.3 mmol/L	25.9	45.5	31.4	57.6[e]
Blood pressure ≥130/85 mm Hg	24.1	54.5	31.4	59.4[e]
Fasting glucose ≥6.1 mmol/L	0	0	1	30.3[e,f]
Metabolic syndrome (≥3 of the former)	1.9	27.3[d]	4.5	33.3[e]

Values are percentages. IR indicates insulin resistance.

[a] *P* < .05 vs control women with BMI <30 kg/m^2.

[b] *P* < .05 vs women with prior GDM with BMI <30 kg/m^2.

[c] The number of women in control and prior GDM groups is lower than in mentioned in A because insulin secretion and resistance indexes were measured in a subset of participants.

[d] *P* < .05 vs control women without insulin resistance.

[e] *P* < .05 vs women with prior GDM without insulin resistance.

[f] *P* < .05 vs control women in the same category of insulin resistance.

Table 5
Predictors of metabolic syndrome and its components at follow-up

Dependent variable	Significant independent variables	OR (95% CI)	ROC area	*P* of the model
A. Logistic regression analysis with metabolic syndrome and its components as dependent variables, and age, GDM or control group, and obesity (BMI ≥30 kg/m²) at follow-up as independent variables				
Waist circumference >88 cm	Obesity	55 (24.6-123)	0.86	<.001
Triglycerides ≥1.7 mmol/L	Obesity	10.65 (3.81-29.7)	0.75	<.001
HDL-C <1.3 mmol/L	Obesity	3.83 (2.15-6.81)	0.61	<.001
Blood pressure ≥130/85 mm Hg	Obesity	4.91 (2.62-9.2)	0.68	<.001
Fasting blood glucose ≥6.1 mmol/L	Obesity	5.33 (1.85-15.39)	0.81	<.001
	Age	1.13 (1.01-1.27)		
	Prior GDM	1478 (0 to 2.2×10^{19})		
Metabolic syndrome (≥3 of the former)	Obesity	22.95 (11.15-68.2)	0.87	<.001
	Age	1.15 (1.04-1.27)		
B. Logistic regression analysis with metabolic syndrome and its components as dependent variables, and age, GDM or control group, and HOMA insulin secretion and resistance as independent variables				
Waist circumference >88 cm	Insulin resistance	9.39 (3.93-22.44)	0.74	<.001
Triglycerides ≥1.7 mmol/L	Insulin resistance	7.7 (1.85-31.97)	0.85	<.001
	Age	1.19 (1.04-1.37)		
HDL-C <1.3 mmol/L	Insulin resistance	2.22 (1.11-4.46)	0.65	.001
	Age	1.07 (1.01-1.14)		
Blood Pressure ≥ 130/85 mm Hg	Insulin resistance	2.62 (1.28-5.34)	0.69	<.001
	Age	1.10 (1.04-1.18)		
Fasting blood glucose ≥6.1 mmol/L	Insulin resistance	184.32 (15.73-2159.69)	0.96	<.001
	Age	1.20 (1.001-1.45)		
	Insulin secretion	0.96 (0.94-0.99)		
Metabolic syndrome (≥3 of the former)	Insulin resistance	10.49 (3.28-33.52)	0.87	<.001
	Age	1.22 (1.07-1.38)		

metabolic syndrome and its components than their non-obese counterparts. The only exception was fasting hyperglycemia, which was not present in control women, either obese or not obese. However, if we refer to women with prior GDM vs those without GDM, no difference was observed.

3.3. Insulin secretion and insulin sensitivity

The subgroup undergoing the insulin secretion and resistance study did not differ from the original group in age or metabolic components (data not shown). Women with prior GDM had a lower insulin secretion (71.8% [16.8-213.4] vs 91.7% [41.5-538.2], $P = .001$) and disposition index (6796 [1766-25 486] vs 8168 [3398-44 713], $P < .001$) than control women, whereas no difference was found in the insulin sensitivity estimation (100.7% [15.1-442.9] vs 90.2% [32.1-218], ns). When the GDM group was split according to the glucose tolerance status, women with abnormal glucose tolerance displayed lower insulin sensitivity (58.2% [15.1-192.6]) than those with normal glucose tolerance (110.7% [29.3-442.9]) and control women ($P = .004$ vs both).

Furthermore, when control women and those with prior GDM were divided in 2 groups according to the presence or absence of insulin resistance (Table 4B), a higher rate of central obesity, triglycerides 1.7 mmol/L or higher, and metabolic syndrome was observed in control women with insulin resistance. Women with prior GDM and current insulin resistance had a higher prevalence of metabolic syndrome and all its components than those without insulin resistance as well as a higher risk of fasting hyperglycemia than control women with insulin resistance. Again, no differences were observed between control women and those with prior GDM in the same insulin resistance category with the exception of fasting hyperglycemia.

3.4. Multivariate prediction of metabolic syndrome

When obesity was included as a potential predictor in the multivariate logistic analysis (Table 5A), it was associated to all components of metabolic syndrome and metabolic syndrome itself. Age contributed to the prediction of metabolic syndrome and hyperglycemia, and prior GDM contributed to the prediction of hyperglycemia. In the multivariate logistic regression analysis using measurements of insulin resistance and secretion among potential predictors (Table 5B), insulin resistance at follow-up was associated to all components of metabolic syndrome and metabolic syndrome itself. The same was true for age with the exception of waist circumference. In addition, insulin secretion was inversely associated with fasting hyperglycemia. According to the receiver operating characteristic (ROC) curves, the ability of the independent variables to predict metabolic syndrome at follow-up was similar when

including GDM and obesity, or HOMA-insulin secretion and sensitivity indexes.

4. Discussion

There is ample evidence that metabolic syndrome, defined as the clustering of metabolic risk factors sharing insulin resistance in its pathogenesis, is associated with an increased risk of cardiovascular disease. Women with GDM have increased blood glucose, lipids, and blood pressure values later in life, but to the best of our knowledge, only 2 papers have reported the prevalence of metabolic syndrome in accordance to NCEP 2001 criteria [8,17].

In agreement with findings in other papers, women with prior GDM in the current study displayed higher blood glucose, blood pressure, VLDL-C, and waist circumference than control women, but we observed no difference in triglycerides and total, HDL, or LDL-C [1,4,8,13]. Again, in agreement with the literature [2,3,9], we found these abnormalities to be more pronounced in women with abnormal glucose tolerance at follow-up, a feature that has also been described in the general population [22,23]. Nevertheless, in our study, when variables were transformed into components of metabolic syndrome according to NCEP 2001 criteria, women with prior GDM only showed a higher rate of fasting hyperglycemia and a trend toward a higher rate of hypertension so that a full-blown picture of metabolic syndrome was not present. It is possible that with a larger study population and/or longer follow-up, differences in the prevalence of metabolic syndrome become significant. However, it is clear that the main difference between women with and without prior GDM is glucose homeostasis. Gestational diabetes mellitus is a predictor of further abnormal glucose tolerance but not of metabolic syndrome.

In the United States, Verma et al [8] reported a prevalence of metabolic syndrome of 27.2% vs 8.2% in the control group at 11 years of follow-up, whereas in Italy, the respective figures were 21.0% vs 4.6% at 8.5 years [17]. The prevalence of metabolic syndrome in women with prior GDM in the aforementioned studies is 2-fold that of our study. The discrepancy of the present study with that of Bo et al [17] is the most intriguing because both were conducted in European Mediterranean countries sharing ethnic and diet characteristics. The different rate of central obesity (twice as high in the study of Bo et al in both the control and study populations) could account for the differences in the other factors.

As to the validity of the groups, women with prior GDM participating in the study had a lower AUC of the OGTT and a lower frequency of previous abnormal glucose tolerance at GDM diagnosis (favoring a less severe abnormality) but an older age (favoring a more severe abnormality) than those nonparticipating. Control group women volunteering for the study had higher blood glucose levels in the 50-g glucose challenge in the third trimester of pregnancy than those who did not, pointing to a higher metabolic risk. However, when we compared the data of the control group with those from the background population of a similar age (35-49 years), no difference was observed with regard to lipid concentrations and blood pressure [24], indicating that the control group was acceptably representative of our population. We can thus say that women with GDM participating in the study were somewhat biased toward normality, whereas the reverse is true for the control group. However, we would like to remark that this information is not provided in similar studies [3,4,8,13]. As potential explanations for this bias, we suggest a higher rate of DM background in control women volunteering for participation, whereas the less severe characteristics in women with GDM could be attributed to the fact that some of the women with more abnormal metabolic characteristics had already been diagnosed of DM at the first assessment after delivery.

With regard to insulin secretion and sensitivity, we report a lower insulin secretion and similar sensitivity in women with GDM vs controls. Most authors have demonstrated that women with GDM have defects in both insulin secretion and sensitivity [11,12,25], but others have reported defects in only the former [26] or the latter [5]. The fact that control women and those with prior GDM differ at follow-up in insulin secretion but not in sensitivity explains that they differ in the rate of fasting hyperglycemia but not in additional components of the metabolic syndrome.

Finally, we have observed that the prediction of metabolic syndrome at follow-up is similar when using in a multivariate analysis either HOMA measures of insulin secretion and resistance or prior GDM and obesity. Most likely, prior GDM operates as a surrogate index of insulin secretion and obesity of insulin resistance. In fact, obesity alone was the main predictor of metabolic syndrome and its components, emphasizing the relevance of this simple clinical variable.

In conclusion, in our population, women with former GDM had similar insulin sensitivity but lower insulin secretion and disposition index than control women. Even when waist circumference, VLDL-C, blood pressure, and OGTT blood glucose concentrations were higher in women with prior GDM, they did not display a distinctly higher prevalence of metabolic syndrome and its components. Therefore, in this population, GDM is a predictor of impaired glucose regulation but not of metabolic syndrome at midterm follow-up. Obesity, a surrogate index of insulin resistance, is the best predictor of metabolic syndrome at follow-up.

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