Dietary fat and gestational hyperglycaemia

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Abstract

Aims/hypothesis. The purpose of this study was to investigate the relation between life-style habits and glucose abnormalities in Caucasian women with and without conventional risk factors for gestational diabetes.

Methods. A total of 126 pregnant women with gestational diabetes, 84 with impaired glucose tolerance and 294 with normal glucose tolerance, identified by sequential screening, were interviewed to determine their usual weekly food pattern, amount of exercise, smoking habits and alcohol intake.

Results. Patients with glucose abnormalities were older and shorter in height and had significantly higher BMI before pregnancy, percentage of diabetic first-degree relatives and higher intake of saturated fat. Patients without known risk factors for gestational diabetes (i.e. younger than 35 years of age, BMI < 25 kg/m², no first-degree diabetic relatives) included 40 with impaired glucose tolerance or gestational diabetes. In a multiple logistic regression model age,

short stature, familial diabetes, BMI and percentages of saturated fat were associated with impaired glucose tolerance or gestational diabetes in all patients, after adjustment for gestational age. In patients without conventional risk factors only percentages of saturated fat (OR = 2.0; 95 %-CI = 1.2–3.2) and polyunsaturated fat (OR = 0.85; 95 %-CI = 0.77–0.92) were associated with gestational hyperglycaemia, after adjustment for age, gestational age and BMI.

Conclusion/interpretation. Saturated fat has an independent role in the development of gestational glucose abnormalities. This role is more important in the absence of conventional risk factors suggesting that glucose abnormalities could be prevented during pregnancy, at least in some groups of women. [Diabetologia (2001) 44: 972–978]

Keywords Gestational diabetes, impaired glucose tolerance, obesity, oral glucose tolerance test, overweight, polyunsaturated fat, risk factors for gestational diabetes, saturated fat.

Gestational diabetes mellitus (GDM) has an incidence of 2–6 % and is associated with maternal morbidity, adverse perinatal outcomes and many other conditions [1–4]. Unmodifiable known risk factors associated with GDM are ethnicity, age, number of pre-

vious pregnancies, and a family history of diabetes. Recently, a short stature has been identified as an independent variable associated with gestational diabetes [5–7]. A modifiable known risk factor is obesity [4]. However, women without conventional risk factors for gestational diabetes also develop the disease [8]. Discovering additional risk factors would help identify those women who need to be tested for gestational diabetes.

Additional modifiable risk factors could be a lack of exercise and dietary fat as well as life-style habits that adversely influence insulin-resistance, such as smoking and certain drugs [4].

Received: 16 January 2001 and in revised form: 23 April 2001

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Abbreviations: GDM, gestational diabetes; P:S ratio, polyunsaturated-to-saturated fat ratio

A lack of exercise seems to be an important risk factor for pregnant women who are obese only [9]. It has recently been shown that women with recurrent GDM had a higher overall intake of fat (as percentage of energy) than those without recurrences [10]. Furthermore, increased polyunsaturated fat intake during pregnancy has been associated with a reduced incidence of glucose intolerance in pregnant Chinese women [11].

Nothing is known about the relation between dietary habits and the impaired glucose metabolism in Caucasian women who are pregnant, or whether lifestyle habits cause gestational glucose abnormalities when conventional risk factors for gestational diabetes are absent.

This study investigates the relation between lifestyle habits and glucose intolerance (IGT) and GDM in Caucasian women with and without conventional risk factors for gestational diabetes.

Subjects and methods

All pregnant women attending the Gynaecological and Obstetrical Department of the University of Torino are routinely screened with a 50 g oral glucose test at 24–28 weeks of gestational age. Gestational age was calculated by ultrasound examination done during the first trimester of gestation. In cases of a positive screening result (1-h serum glucose concentration ≥ 7.8 mmol/l), a 3-h oral glucose tolerance test (OGTT) with 100 g glucose was administered after 1–2 weeks. The test was done in the morning after an overnight fast of at least 8 h but not more than 14 h and after at least 3 days of an unrestricted diet (≥ 150 g carbohydrates/day) and exercise, using cut-off values previously proposed [12] for the extrapolation of the whole blood glucose values to plasma or serum glucose concentrations [13]. GDM was diagnosed in women with two serum glucose concentrations above the following levels 5.3 mmol/l (fasting), 10.0 mmol/l (1 h), 8.6 mmol/l (2 h), 7.8 mmol/l (3 h). If only one glucose value was higher than these cut-off levels IGT was diagnosed.

Subjects selection was made on the basis of a sequential screening from April 1999 to November 2000. Pregnant women known to have diabetes mellitus or a disease affecting glucose metabolism were excluded. A total of 126 women with GDM and 84 with IGT were identified. All consecutive subjects (294 women) with normal glucose tolerance during the first month of this period served as the control subjects. All participants gave their informed consent and all the procedures followed were in accordance with the Helsinki Declaration of 1975.

Height was measured at the time of the screening and patients gave information on their pre-pregnancy weight. The body mass index (BMI) was calculated as pre-pregnancy weight in kilograms divided by the square of the height in meters.

Overweight and obesity were defined as BMI of 25 kg/m² or more and less than 30 kg/m² and a BMI of 30 kg/m² or more, respectively. The following were taken as the conventional risk factors for gestational diabetes: an age higher than 35 years, BMI higher than 25 kg/m² and a first-degree relative with Type II (non-insulin-dependent) diabetes mellitus. Using

these criteria, 173 patients were without risk factors and 40 of them had IGT or GDM (23 %).

All women were asked whether any members of their families (living or not) had or had had diabetes as diagnosed by a physician. Patients with a diabetic mother, father, brother or sister were considered as having an affected first-degree relative. Usual physical activity during both work and leisure was evaluated according to methods previously described [14]. Arbitrary scores were assigned to degrees of physical activity during work (not working = 0, mainly sitting = 1, sitting or standing = 2, walking/handling materials = 3) and leisure (inactive = 1–4 h a week of physical activity = 2, regular physical activity = 3). The sum of the two scores was combined and three levels of physical activity were considered: vigorous (score 5–6), moderate (score 3–4), light (score 1–2).

Smoking habits for former and currently smoking women (number of cigarettes a day; years of smoking) were recorded. Mean daily and weekly alcohol intake and kinds of beverages were obtained by interview.

A list of foods was designed based on a semiquantitative food-frequency questionnaire previously described [15]. We aimed to categorize individuals according to their intake of classes of nutrients to verify the occurrence of an event – gestational hyperglycaemia – closely related to a short-lasting event – pregnancy and therefore we adapted the previously described approach. Unlike the previous study [15] our subjects were Europeans and we did not test the effect of selected nutrients on the occurrence of chronic conditions (e.g. cancer or heart disease) or undertake a “past year evaluation” of dietary intake because women frequently change their dietary habits in pregnancy (more “healthy” habits, avoidance of some foods, etc.). Instead, we prepared a list of foods more frequently consumed in Northern Italy in consultation with an experienced dietician (FDM). For each item, different portion sizes were specified. All women were interviewed by three physicians trained in assessing habitual food patterns (blinded to the results of the OGTT), using the food lists. The women were asked to indicate how often a day and how many days a week they had consumed the specific amount of each food during the last week and in what portions; using photos to compare portions. Data on cooking methods was also collected. Data from the food lists completed by the physicians was entered into a software programme (Food Meter, Medimatica, Martinsicuro, Teramo, Italy 1990, modified in 1998 in our University according to the table of food consumption of the Italian National Institute of Nutrition [16]). The database contained all foods consumed by the study cohort.

The reliability of the reported energy intake was assessed by calculating the ratio of estimated energy intake to predicted basal metabolic rate using age- and sex-specific formulas derived by Schofield [17]. The cut-off value of less than 0.88, representing the 97.5 %-CI, was used as evidence of underreporting [18]. The eighteen under-reporters (3.6 %), according to this formula, were equally distributed in the three categories of glucose tolerance.

Serum glucose was measured by the glucose oxidase method (Glucose-Analyzer II Beckman, Fullerton, Calif., USA). Fasting insulin was measured by radioimmunoassay (Corning Kit, Modfield, Mass., USA); the coefficients of variations were 3.4–5.1 %.

Analysis of variance and chi-square test were used to compare means for continuous variables or frequencies for discrete variables. ANCOVA (analysis of covariance) was used to compare different continuous variables, using BMI as a covariate. Linear correlations were performed to evaluate the association of BMI with dietary variables. Multiple regression analyses

Table 1. Clinical characteristics of the patients studied

	Normoglycaemia	IGT	GDM	<i>p</i>
Patients (<i>n</i>)	294	84	126	
Age (years)	31.8 ± 4.4	33.0 ± 4.9	33.0 ± 4.8	0.02
Weight (kg)	62.8 ± 13.3	67.9 ± 15.1	66.7 ± 15.4	0.003
Height (m)	1.63 ± 0.07	1.61 ± 0.06	1.62 ± 0.06	0.02
BMI (kg/m ²)	23.6 ± 4.6	26.0 ± 5.5	25.4 ± 5.3	0.00002
Nulliparous (%)	62	57	55	NS
Smoking (%)	27	25	33	NS
Familial diabetes (%) ^a	28	33	41	0.04
Physical activity:				
Light (%)	21	21	24	NS
Moderate (%)	65	66	67	NS
Vigorous (%)	14	13	9	NS
Fasting insulin (pmol/l)	72.0 ± 75.6	130.2 ± 187.2	116.4 ± 186.0	0.0081 ^b

^aFirst-degree relatives^bAfter adjustment for BMI**Table 2.** Nutritional data obtained by dietary assessment

	Normoglycaemia	IGT	GDM	<i>p</i>
Alcohol (gr/day)	2.98 ± 7.4	1.78 ± 6.7	3.78 ± 7.7	NS
Total energy (kcal)	2035 ± 627	2002 ± 568	1889 ± 490	NS
Fat (%kcal)	31.8 ± 7.6	33.1 ± 7.4	33.6 ± 9.1	NS
Protein (%kcal)	14.8 ± 2.5	14.9 ± 2.9	14.3 ± 2.4	NS
Carbohydrate (%kcal)	52.6 ± 7.7	51.6 ± 8.2	51.2 ± 9.0	NS
Complex carbohydrate (% total carbohydrates)	58.8 ± 11.1	59.0 ± 13.5	57.3 ± 12.8	NS
Fat (% total fat)				
Saturated	34.4 ± 6.7	35.8 ± 8.3	36.5 ± 11.0	0.04
Polyunsaturated	21.8 ± 5.0	21.3 ± 3.7	20.7 ± 4.7	NS
Monounsaturated	43.8 ± 3.8	42.8 ± 5.9	42.8 ± 7.1	NS
Fat (% total kcal)				
Saturated	10.9 ± 3.1	11.7 ± 3.1	12.0 ± 4.4	0.004
Polyunsaturated	6.9 ± 2.2	7.1 ± 2.1	7.0 ± 2.7	NS
Monounsaturated	14.0 ± 3.9	14.3 ± 4.2	14.5 ± 4.9	NS
P:S ratio	0.70 ± 0.51	0.64 ± 0.22	0.63 ± 0.25	NS
Fiber (gr)	16.4 ± 5.3	16.3 ± 4.6	15.2 ± 4.9	NS

Table 3. Multiple logistic regression analyses evaluating the association of IGT/GDM with the variables listed in all patients and in those without first-degree diabetic relatives, not overweight and younger than 35 years of age (right column)

Independent variables	All patients (<i>n</i> = 504)	Without risk factors (<i>n</i> = 173)
	OR; 95 %-CI; <i>p</i>	OR; 95 %-CI; <i>p</i>
Age	1.3 ^a ; 1.1–1.6; 0.008	0.8 ^a ; 0.5–1.3; NS
Height	0.7; 0.5–0.9; 0.03 ^b	0.6; 0.3–1.1; NS ^b
Familial diabetes ^c	1.5; 1.1–2.3; 0.03	1.5; 0.7–3.2; NS
Classes of BMI ^d	1.8; 1.3–2.3; 0.00002	
Saturated fat (% total fat)	1.3 ^e ; 1.1–1.6; 0.02	2.0 ^e ; 1.2–3.2; 0.007
Polyunsaturated fat (% total fat)	0.96; 0.92–1.00; NS	0.85; 0.77–0.92; 0.003

^aFor each five years of age increase^bFor each 10 cm increase^cDiabetes in any relative^dNormal weight (BMI < 25 kg/m²) ; overweight (BMI ≥ 25 and < 30 kg/m²); obesity (BMI ≥ 30 kg/m²)^eFor 10 % increase of saturated fat

were performed to analyse correlations between the polyunsaturated-to-saturated (P:S) fat ratio and fasting insulin, and correlations between fibre intake and presence of IGT/GDM, after multiple adjustments. Multiple logistic regression analysis based on the maximum-likelihood method was performed to determine the independent contribution of BMI, height, age, familial diabetes and percentages of total, saturated, monounsaturated and polyunsaturated fat on the presence of IGT and GDM.

As insulin values were not normally distributed, they were log-transformed. Data are presented as means ± standard deviation or percentages in Table 1 and Table 2 and as odds ratios (OR) and 95 %-CI in Table 3. A *p* value of less than 0.05 was considered significant.

Results

Patients with IGT and GDM were older and had significantly higher pre-pregnancy weights and BMI, short stature and a more frequent history of diabetes in first-degree relatives (Table 1). No significant differences were found for number of pregnancies,

smoking habits and levels of exercise. In smoking patients, neither the number of cigarettes/day, nor the years of smoking were significantly different in the three groups. Moreover, there were no significant differences between the three groups in total energy and fat, protein and carbohydrate intake, expressed as a percentage of total energy and complex carbohydrates (expressed as a percentage of total carbohydrates) (Table 2). Data did not change, after adjustment for BMI. The women with IGT and GDM, considered as a single group, displayed a significantly higher fat intake (as % total kcal) than the control subjects ($p = 0.03$). Alcohol intake was not significantly different in the three groups. Interestingly, IGT and GDM patients ate a significantly higher percentage of saturated fat (% total fat). This difference was still significant, when saturated fat was expressed as percentage of total kilocalories (Table 2). The P:S ratio decreased progressively from normoglycaemic to diabetic women, though not significantly.

Fiber intake differed only between patients with GDM and normoglycaemic patients. However, in a multiple regression model, fibre intake was slightly negatively related to the presence of IGT/GDM, after adjustment for age, BMI, familial diabetes, height and percentage of saturated fat ($\beta = -0.008$; 95 %-CI = -0.017 – 0.0003 ; $p = 0.043$).

There was no significant relation between BMI and lipids, carbohydrates, proteins, expressed as a percentage of Kcal, and saturated, monounsaturated and polyunsaturated fat intakes, expressed as a percentage of total fat.

In patients without risk factors for gestational diabetes, either with IGT/GDM ($n = 40$) or with normal glucose tolerance ($n = 133$), we evaluated the intakes of saturated and polyunsaturated fats (as a percentage of total fat), expressed as tertiles (respectively, lower, middle and higher tertile). A higher percentage of patients with IGT/GDM showed a higher intake of saturated fat (respectively: 55 %, 40 %, 5 % for the higher, middle and lower tertiles) and a lower intake of polyunsaturated fat (respectively: 10 %, 40 %, 50 % for the higher, middle and lower tertiles) than the normoglycaemic women (respectively $p = 0.01$ for saturated fat and $p = 0.02$ for polyunsaturated fat). Moreover, the 40 women with IGT/GDM without risk factors showed a lower P:S ratio, when compared to the 133 normoglycaemic patients (respectively 0.49 ± 0.17 vs 0.73 ± 0.72 ; $p = 0.04$) (Fig. 1). No significant differences were evident for fibre intake, alcohol consumption, smoking habits or exercise in IGT and GDM women without risk factors for gestational diabetes compared with the normoglycaemic women without risk factors.

All patients with an intake of more than 30 % of saturated fat as a percentage of total kilocalories ($n = 11$) had IGT or GDM (data not shown). A similar cut-off was not evident for polyunsaturated fat.

Fig. 1. P:S ratio in women without conventional risk factors for gestational diabetes (less than 35 years of age, without first-degree diabetic relatives and not overweight) respectively with IGT/GDM (left) and with normal glucose tolerance (right)

In a multiple logistic regression model, age, lower height, familial diabetes, BMI and percentages of saturated fat (percentage of total fat) were all associated with the presence of IGT/GDM (Table 3), after adjustment for gestational age. In patients with a BMI of less than 25 kg/m², younger than 35 years of age and without diabetes in their first-degree relatives, only the associations with percentages of saturated fat (OR = 2.0; 95 %-CI = 1.2–3.2, $p = 0.007$) and percentages of polyunsaturated fat, as a percentage of total fat, (OR = 0.85; 95 %-CI = 0.77–0.92; $p = 0.0035$) remained significant, after adjusting for age, gestational age and BMI (Table 3). No significant associations were evident for monounsaturated fat (as % fat), percentages of total fat (as % kcal), after adjusting for age, BMI classes, familial diabetes, gestational age and height.

Fasting insulin values were higher in women with IGT/GDM, after adjustment for BMI (Table 1) and increased from the lowest to the highest tertiles of intake of saturated fat both in all women (respectively, 80.4 ± 81.6 , 89.4 ± 148.8 and 106.8 ± 160.8 , $p = 0.012$) and in lean women (respectively, 63.6 ± 60.6 , 75.0 ± 133.2 and 92.4 ± 124.8 , $p = 0.009$), after adjustment for BMI. Furthermore the P:S ratio was an independent predictor of fasting insulin values, after adjustment for age, BMI and glucose tolerance status, in a multiple regression model ($\beta = -0.34$; 95 % CI -0.50 – 0.18 ; $p = 0.00006$).

Discussion

Our data provides evidence of the independent role of known risk factors for gestational diabetes, such as age, overweight or obesity and family history of diabetes on glucose abnormalities of Caucasian women between 24 and 30 weeks of pregnancy [4]. About 20% of our IGT/GDM patients had no conventional risk factors for gestational diabetes justifying the search for other conditions to explain these metabolic abnormalities.

No relevant association was evident with parity. Increasing parity has been found to have little or no effect on the risk of Type II diabetes, after adjustment for other risk factors in large population studies [19–21].

Shortness of stature, even if the difference in height between the groups was quite small, was an independent predictor of IGT/GDM, as shown by previous studies [5–7]. A possible explanation of this association could be reduced fetal growth, which was reported to be associated with insulin resistance in adult life and with impaired glucose tolerance in pregnancy [22–23]. The association between lower height and IGT/GDM, however, was not significant in the group of women without risk factors for gestational diabetes (Table 3), or in the normal-weight women ($BMI < 25 \text{ kg/m}^2$) (data not shown) in a multiple logistic regression model. These results agree with the prevalent association of short stature with gestational diabetes in women with a greater mass of fat [7] supporting the hypothesis that low birth weight predisposes to obesity, reduced height and insulin sensitivity in the adult life [24–25].

The percentage of fat intake was higher in the group with IGT and GDM when compared with women with normal glucose tolerance. However, after adjustment for multiple variables, no significant association was evident. Moreover, BMI and intake of fat or its subtypes were not correlated. The results of human studies on this topic have been conflicting and a recent analysis of the NHANES I Epidemiologic Follow-up Study shows a very weak correlation between baseline percentage of fat intake and subsequent weight change in the subsequent 8 to 10 years [26–27].

The percentage of saturated fat was an independent predictor of metabolic abnormalities in our patients and the fact that the few women with an exceptionally high consumption of saturated fat (30% of total kilocalories) all had glucose abnormalities is an intriguing confirmation of this conclusion. According to the literature, a higher proportion of polyunsaturated fat is associated with enhanced insulin action. Particularly a high intake of n-3 polyunsaturated fat in respect to n-6 polyunsaturated fat confers greater protection [26]. Unfortunately, we could not separate n-3 and n-6 polyunsaturated amount with our data-

base. The lower intake of polyunsaturated fat was negatively associated with abnormal oral glucose tolerance tests only in our lean and younger women without first-degree diabetic relatives. This suggests that life-style conditions play an important independent part in the absence of other conditions associated with insulin resistance. The role of monounsaturated fat intake is not so clear but appears to be more like saturated fat [28]. In our patients, no significant role was evident for monounsaturated fat, even if its intake was much higher than in other populations because most of our patients used only olive oil [10–11].

Our findings agree with recent data on dietary fat subtypes and insulin resistance [26, 29] supporting a link between higher saturated fat intake and insulin resistance, progression to glucose intolerance and diabetes. In fact, a high proportion of long-chain unsaturated fatty acids and a low proportion of saturated fatty acids in the phospholipids of the skeletal muscle membranes have been related to a high insulin sensitivity and seem to affect the glucose-stimulated insulin secretion [30–31]. In line with this data, fasting insulin values in our subjects increased with the higher intake of saturated fat and were inversely related to the P:S ratio, even after adjustment for the glucose tolerance status, suggesting a role for dietary fatty acids in the metabolism of insulin.

As recently reported, postprandial glucose concentrations in women who are pregnant are associated with worse perinatal outcomes [32]. Reducing the amount of carbohydrates and increasing slightly the amount of fat have thus been recommended to lower postprandial glycaemic spikes. According to our results, it would, however, be necessary to increase only the proportion of polyunsaturated fat of pregnant women.

Our data is in line with those obtained from a Chinese population with a very different dietary pattern [11]. Soy oil contributed to about 70% of the total polyunsaturated fat of the Chinese women whereas in our women olive oil was principally used, explaining their higher intake of monounsaturated fat. The fact that congruent results have been obtained in two disparate populations greatly strengthens the probability that dietary fat composition is an important and easily manipulated lifestyle variable in the causation of gestational diabetes.

The most intriguing and never reported finding is that lean and younger women without diabetic first-degree relatives show a significant association between lipid subtypes and IGT/GDM during pregnancy (Table 3; Figure 1). A very low percentage of individuals without conventional risk factors with IGT/GDM ate the lowest amount of saturated fat (5%) or the highest amount of polyunsaturated fat (10%) and their P:S ratio was the lowest (Fig. 1). Therefore in the absence of the conventional risk factors for gestational diabetes, environmental conditions could be-

come relevant. This is in line with the finding that also lean and younger women can develop GDM [8]. Thus, in this group a higher intake of polyunsaturated fat appeared to be protective, in agreement with previous studies [11, 26, 28]. This data could help prevent this complication, at least in this group of women.

A slight protective role of fibre intake was found in women with conventional risk factors for gestational diabetes, in agreement with studies which found a protective role for fibre intake and incidence of Type II diabetes in women, above all in those overweight and obese [33–34].

There are, of course, some limits to dietary interviews. But because most of these women were cooking and buying foods themselves for their families, they were the best sources of data about portions of food, amount and kind of condiments and cooking practices.

There was no significant association between smoking habits, alcohol intake, exercise and glucose abnormalities in pregnancy. We are aware that our scores for physical activity were arbitrary but they have been already validated by previous studies including our own [14, 35–37]. There was an association, though not significant, for exercise: a higher percentage of inactive and a lower percentage of active women had IGT/GDM (Table 1). It is possible that this association could be revealed to be significant using a more appropriate definition of physical activity. Exercise, in fact, seems associated with reduced rates of GDM particularly in obese women [9] in line with data of literature showing a protective effect of physical activity on the risk of Type II diabetes in women [38–39].

In conclusion, our data show the independent role of saturated fat on the development of gestational glucose abnormalities, especially in women with normal weight, under 35 years of age and without first-degree diabetic relatives, a group for whom, moreover, a higher intake of polyunsaturated fat seems protective. Corroboration of these results in prospective interventional studies on diets with low saturated and high polyunsaturated fats could help prevent glucose abnormalities during pregnancy and their adverse effects on both the mother and the child, at least in some groups of women.

Acknowledgements. We are indebted to Dr R. Arcari for her valuable assistance in the revision of the manuscript.

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