ORIGINAL ARTICLE

Blood pressure and lipid changes in gestational diabetes mellitus

Monika Szymanska, Dorota A. Bomba-Opon, and Miroslaw Wielgos

1st Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland

Correspondence to: Monika Szymanska, PhD
1st Department of Obstetrics and Gynaecology
Medical University of Warsaw, Pl. Starynkiewicza 1/3, 02-015 Warsaw
tel. +48 22 5021430; fax +48 22 5022157
email: mszym@amwaw.edu.pl

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Abstract

OBJECTIVE: It is suggested that gestational diabetes mellitus (GDM) is the earliest phase of DM. Nowadays DM is treated as a part of insulin resistance syndrome – patients with DM tend to be obese, dyslipidemic and hypertensive. It is postulated that similar abnormalities are found in GDM patients.
METHODS: The study was conducted among 81 women with GDM and 41 healthy controls. After diagnosis or negative screening for GDM the women underwent 24-hour blood pressure monitoring and measurements of plasma lipids, insulin concentrations and insulin resistance (expressed by HOMA score). The incidence of gestational hypertension and blood pressure until delivery was also analyzed.
RESULTS: 17 (21%) of GDM women and only 1 glucose tolerant control developed pregnancy induced hypertension. GDM women had significantly higher arterial pressure during the daytime and nighttime (accordingly 112.1/69.4 mmHg vs. 105.4/64.8 mmHg and 101.5/62.4 mmHg vs. 93.0/58.8 mmHg), although the average BP was within normal range. Heart rate was also faster in GDM group. Compared with healthy pregnant women, GDM patients had higher serum TG concentrations (247,9 vs 205 mg%; p<0,01), fasting insulin (66 vs 42,5 pmol/l; p<0,001) and insulin resistance (HOMA 2,15 vs 1,13; p<0,001). No correlation was found between blood pressure and insulin concentrations and insulin resistance among healthy and GDM women.
CONCLUSIONS: The results suggest that symptoms of insulin resistance are present in GDM women. They are characterized by higher arterial blood pressure, heart rate, serum triglycerides, insulin and increased insulin resistance.

INTRODUCTION

Gestational diabetes mellitus (GDM) is characterized as any degree of glucose intolerance first detected in pregnancy. It occurs in 2 to 3,8% of Polish women (Wojcikowski et al., 2002). The disease is more common among Latin women and Afro-Americans than among women with white origin. It is assessed that even as many as 15% of Latin and Afro-American women have GDM (King, 1998). The disease is caused by the increased insulin resistance, diminished insulin sensitivity and impaired insulin secretion. There are no typical symptoms of diabetes. A woman feels healthy and has no information of the disease. Although mild intolerance of carbohydrates is not dangerous for pregnant women, it is for the fetus. Fetal hyperglycemia causes exaggerated fetal insulin secretion.

Abbreviations

BMI – body mass index
CH – total cholesterol
DBP – diastolic blood pressure
ECLIA – electrochemiluminescence immunoassay
GCT – glucose challenge test
GDM –gestational diabetes mellitus
HDL-CH – high-density lipoproteins cholesterol
HOMA – homeostasis model assessment
HR – heart rate
IRS – insulin resistance syndrome
IDF – International Diabetes Federation
LDL-CH – low-density lipoproteins cholesterol
MAP – mean arterial pressure
OGTT – oral glucose tolerance test
SBP – systolic blood pressure
TG – triglycerides

Hyperinsulinemia is considered to be one of the most important mechanisms contributing to fetal macrosomia, neonatal hypoglycaemia, delayed lung maturation and respiratory disorders. Elevated plasma free fatty acids can also influence fetal growth (Bomba-Opon D. et al., 2006)

GDM usually resolves after delivery, but the women are predisposed to the development of type II diabetes mellitus (DM) in the future life. Studies estimate that even 45% of women with a history of GDM will develop impaired glucose tolerance or DM within 7 years after pregnancy (Kousta et al., 1999). GDM might be a risk factor for type I diabetes in the offspring (Dörner G. et al., 2000).

Nowadays DM is treated not as a single disease, but as a part of a syndrome of insulin resistance. It is commonly manifested with obesity, lipid abnormalities and hypertension. Some studies have demonstrated similar abnormalities among GDM patients. They tend to have higher levels of triglycerides and lower levels of HDL cholesterol. It is also listed that GDM patients have higher systolic and diastolic blood pressure in the second trimester of pregnancy. Consequence of insulin resistance in the increase of blood pressure is under consideration.

In the prospective study pregnant women with GDM and glucose tolerant underwent detailed studies of arterial pressure, lipid concentrations, insulin levels and insulin resistance. We postulated that features related to metabolic syndrome (insulin resistance, dyslipidemia, hypertension) are correlated with incidence of gestational diabetes mellitus. We hypothesized that GDM is not a single disease, but a part of insulin resistance syndrome occuring, for the first time during pregnancy.

MATERIAL AND METHODS

The study was conducted among 81 women with gestational diabetes mellitus (GDM group) and 41 healthy controls (control group). The women were recruited from patients of 1st Clinic of Obstetrics and Gynaecology Medical University of Warsaw.

GDM was diagnosed on a basis of fasting glucose, 50-g glucose challenge test (GCT) or 75-g oral glucose tolerance test (OGTT). Fasting glucose above 124mg/dl, recorded twice, was considered abnormal and the woman had GDM diagnosed. Abnormal result of GCT was defined as a 1-h glucose value of 200mg/dl or more. If the 1-h glucose value was between 140 and 199 mg/dl, OGTT was conducted as soon as possible. The criteria for OGTT were: fasting glucose of 100 mg/dl, 1-h 180mg/dl, and 2-h 140mg/dl. GDM was diagnosed by one or more abnormal values. The testing in study group was performed between 15 and 33 weeks gestation, on average in 27,8 week. It was performed before 24 weeks gestation, if fasting plasma glucose level was abnormal.

All the patients from control group were negatively screened for GDM – first trimester fasting glucose level below 100 mg/dl and below 140mg/dl in GCT (on average in the 26 week of pregnancy; between 24 and 29 weeks).

The criteria for exclusion from the study were: history of hypertension, heart and renal disease or prepregnancy diabetes.

All GDM women were placed on a diabetic diet with contence of 40% carbohydrate, 40% fat and 20% protein. They were equipped with glucometers (Precision, Abbott) and were monitoring their blood glucose 4 times a day: fasting and 1 hour after each main meal. The diet should assure normal glucose values: fasting < 100 mg/dl; postprandial < 140 mg/dl and during the night 60–90 mg/dl. If the targeted values of glucose could not be reached with the diet, insulin treatment was initiated (11 women). Intermediate-acting biosynthetic human insulin (Ultratard, Novo Nordisk) was used to normalize fasting glucose and short acting insulin before main meals.

Before the initiation of the study patients were informed about the study and all of them provided written consent. The authors obtained consent for the study from The Ethical Committee of Medical University of Warsaw.

After diagnosis or negative screening for GDM the women were hospitalized in the clinic for further investigations. They underwent measurements of plasma lipids (CH, LDL-CH, HDL-CH, TG), insulin concentrations and insulin resistance. Measurements of plasma lipids were performed using Thermo Electron Corporation diagnostic sets. Insulin was measured by ECLIA method, using Roche sets. Insulin resistance was expressed by HOMA score:

HOMA = fasting glucose [mmol/l] × fasting insulin [μU/ml] / 22,5.

At the beginning of the study each woman underwent 24-hour blood pressure monitoring. We had chosen

Table 1. Patient characteristics.

	GDM (n=81)			Controls (n=41)			p
Age [years]	29.84	±	0.49	28.54	±	0.58	—
Height [m]	1.64	±	0.01	1.64	±	0.01	—
Prepregnancy weight [kg]	70.09	±	1.98	62.32	±	1.73	p<0.01
Prepregnancy BMI [kg/m^2]	25.94	±	0.73	23.15	±	0.56	p<0.01
Prepregnancy BMI > 27 [kg/m^2]	32.1%			4.9%			p<0.001
Weight gain							
Till the time of research [kg]	8.95	±	0.51	9.96	±	0.49	—
From the time of research till the delivery [kg]	2.56	±	0.24	5.17	±	0.38	p<0.001
In pregnancy [kg]	11.51	±	0.53	15.13	±	0.62	p<0.001
Nulliparous	55.6%			65.9%			—

that method of blood pressure (BP) measurements because it is much more accurate and representative than individual measurement made by a physician. It also shows day and night rhythm of arterial pressure, which may be altered in some diseases, for example in hypertension. Additionally, the highest BP levels may occur during the night. 24-h blood pressure monitoring was assessed using Medilog (Oxford) device. The monitoring was started at 10.00 a.m. and ended at 10.00 a.m. on the following day, the intervals between the readings were 30 minutes. As a day time BP we defined readings made from 6.00 a.m. to 10.00 p.m. and night time BP – from 10.00 p.m. to 6.00 a.m. MAP (mean arterial pressure) was calculated as: [SBP + 2 × DBP] / 3. At each subsequent visit (every 3 weeks) BP was measured using the same sphygmomanometer. Gestational hypertension (GH) was defined as SBP of > 140 mmHg and DBP > 90 mmHg measured at least two times, at least 6 hours apart. The incidence of gestational hypertension and blood pressure until the end of pregnancy was also analyzed.

Patients' demographic information, such as age and parity were recorded. Prepregnancy weight was obtained from patients medical records. The women were weighed out at the time of research and before the delivery. Body mass index (BMI) was calculated as:

BMI [kg/m^2] = Maternal weight [kg] / Height × Height [m^2]

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS). Results are expressed as means ± fault. Differences between the groups were analyzed by Student's T-test. Results were considered statistically significant with p<0,05. To examine relationship MAP and insulin concentrations or MAP and insulin resistance least squares method was used.

RESULTS

As can be seen from Table 1 GDM patients were more likely to be obese before and during the pregnancy. 32,1% of them were obese (BMI>27 kg/m^2) comparing with 4,9% of glucose tolerant. The pregnancy weight gain until the time of research was similar in the groups. However, weight gain from the time of research until the delivery was higher among controls. Majority of the women were nulliparous.

24-hour blood pressure monitoring which was carried out on average in the 28th week of pregnancy revealed significant differences between the groups. GDM women had significantly higher arterial pressure during the daytime and nighttime (112.1/69.4 mmHg vs. 105.4/64.8 mmHg and 101.5/62.4 mmHg vs. 93.0/58.8 mmHg, respectively), although the average BP was within normal range. Heart rate was also faster in GDM than in control group (Table 2). Circadian pattern of blood pressure was preserved in the groups. During the night reduction of systolic (SBP) and diastolic blood pressure (DBP) was observed. 32.1% of study group were characterized by pre-pregnancy BMI>27 kg/m^2 comparing with 4.9% among the controls. This difference between the levels of blood pressure remained in later course of pregnancy until delivery (Table 3). 17 (21%) of GDM women and only 1 (2.4%) glucose tolerant control developed gestational hypertension.

Compared with healthy pregnant women, GDM patients had significantly higher serum TG concentrations (247.9 vs 205 mg%; p<0.01). There was no statistical difference between total, HDL and LDL cholesterol. Fasting insulin and insulin resistance were also significantly higher in GDM group (Table 4).

Relationship between MAP and insulin level or HOMA score was also analyzed. However, the correlation between blood pressure and insulin concentrations or blood pressure and insulin resistance was found neither among healthy nor GDM women (Table 5).

Table 2. Blood pressure [mmHg] and heart rate [1/min] during 24-hour blood pressure monitoring on average in the 28th week of pregnancy in GDM and control group (results expressed as mean ± fault)

	GDM (n=81)			Controls (n=41)			p
Day							
SBP	112.12	±	0.87	105.39	±	1.25	p<0.001
DBP	69.44	±	0.70	64.76	±	0.99	p<0.001
MAP	83.67	±	0.69	78.30	±	0.97	p<0.001
HR	89.25	±	0.83	79.95	±	0.97	p<0.001
Night							
SBP	101.54	±	0.90	92.98	±	0.82	p<0.001
DBP	62.41	±	0.78	58.83	±	0.90	p<0.01
MAP	75.45	±	0.71	70.21	±	0.80	p<0.001
HR	78.00	±	0.84	68.15	±	1.02	p<0.001
Difference between day and night							
SBP	10.58	±	0.66	12.41	±	0.86	—
DBP	7.04	±	0.61	5.93	±	0.99	—
HR	11.25	±	0.60	11.80	±	0.82	—
MAP	8.22	±	0.51	8.09	±	0.77	—

DISCUSSION

It is well known that intrauterine exposure to gestational diabetes can have important consequences for a fetus and a newborn. It has also been recognized that the effect extends beyond that apparent at birth and results in higher rates of obesity, impaired glucose tolerance and diabetes mellitus in later life of an offspring. For the women, GDM during pregnancy may predispose to the development of diabetes mellitus. Conversion rate from GDM to impaired glucose tolerance or DM can vary from 11% to 45% (Conway et al., 1999; Kousta et al., 1999), depending on the diagnostic criteria and the time of observation.

Nowadays DM is treated no longer as a disease alone, but as a part of a syndrome of insulin resistance. International Diabetes Federation (IDF) defined the syndrome as a coexistence of obesity and two of four factors: raised TG, reduced HDL-CH, raised blood pressure above 130/85 mmHg and any degree of glucose intolerance. It is estimated that as many as a quarter of the world's adults have metabolic syndrome. They are twice as likely to die and three times as likely to have a heart attack or stroke compared with people without the disease. A few studies have suggested the incidence of metabolic disorders connected with IRS among women with GDM.

In this prospective study we compared some metabolic components of IRS syndrome and blood pressure among women with GDM and healthy controls. Most of the investigations were carried out in the early third trimester, just after diagnosis or negative screening for GDM. All the women had proved normal blood pressure during the first trimester of the pregnancy. We showed that women with GDM were characterized by higher BMI, higher insulin and triglyceride levels. Insulin resistance was expressed by HOMA score. It was proved that during pregnancy, results of the method were well correlated with the insulin resistance estimated by euglycemic clamp studies (Kirwan et al., 2001). The GDM women were more insulin resistant than non-GDM. We also noted that the diabetic women had higher CH and HDL-CH levels and lower LDL-CH levels. However, the difference wasn't of statistical significance. The women with glucose intolerance had also higher SBD, DBP and HR at the baseline and during futher observation. 21% of them developed gestational hypertension or preeclampsia comparing with 2.4% of controls.

At the time of GDM diagnosis we found almost all the elements that IRS consists of.

Our results are similar to the Clark's et al. study (1997). Clark, for the first time, suggested that GDM should be added to the list of components of insulin resistance syndrome. He proved that independently of obesity, TG, HDL-CH, free fatty acids and insulin levels were correlated with the diagnosis of GDM. Contrary to the Clark's study, we compared GDM women with healthy controls, negatively screened for GDM. His study based on a population of women initially positively screened for GDM.

The most common threats connected with metabolic syndrome are cardiovascular diseases. In pregnant women a relationship between glucose levels and BP has already been found. Run et al. (2001) showed positive correlation between 2-h OGTT results and MAP in the third trimester of pregnancy. The correlation was independent of prepregnancy or gestational BMI and existed also when MAP was within normal range.

Many other studies proved that GDM is a risk factor of gestational hypertension (Berkowitz et al., 1992; Garner et al., 1990; Greco et al., 1994; Kvetny et al., 2003; Nordlander et al., 1989; Vambergue et al., 2002). Garner

Table 3. Blood pressure [mmHg] in the course of pregnancy in GDM and control group (results expressed as mean ± fault)

	GDM (n=81)			Controls (n=41)			p
SBP							
28 hbd	110.39	±	0.82	105.39	±	1.25	p<0.001
34 hbd	115.08	±	1.08	111.34	±	1.54	p<0.01
Before delivery	120.00	±	1.08	111.10	±	3.12	p<0.001
DBP							
28 hbd	68.38	±	0.64	64.76	±	0.99	p<0.001
34 hbd	71.72	±	0.94	67.93	±	1.18	p<0.001
Before delivery	74.73	±	0.87	69.39	±	2.16	p<0.001

Table 4. Lipid profile, insulin and insulin resistance (HOMA score) in GDM and control group (results expressed as mean ± fault)

	GDM (n=81)			Controls (n=41)			p
CH [mg/dl]	250.8	±	3.8	246.0	±	7.5	—
LDL [mg/dl]	118.5	±	3.1	127.8	±	5.2	—
HDL [mg/dl]	81.6	±	1.8	77.2	±	2.6	—
TG [mg/dl]	247.9	±	8.3	204.9	±	10.3	p<0.01
Insulin [pmol/l]	66.0	±	5.0	42.46	±	2.24	p<0.001
HOMA	2.15	±	0.17	1.13	±	0.06	p<0.001

Table 5. Correlation Coefficients (r) between MAP with serum insulin and HOMA in GDM and control group.

	GDM (n=81)	Controls (n=41)	p
Insulin	0.12	0.16	—
HOMA	0.04	0.24	—

and al. (1990) found 7.8% of GH in women with GDM comparing with 4.3% in glucose tolerant. Berkowitz et al. (1992) showed similar dependence between GDM and preeclampsia. Kvetny et al. (2003) compared GDM and non GDM women characterized by similar MAP at the entry – 85 mmHg and found three times higher occurrence of hypertension, but not preeclampsia. Values of IGFBP-1, high in patients with glucose intolerance, are significantly higher in women with hypertension in pregnancy and preeclampsia, specially connected with IUGR. Another study showed (Caruso et al., 1999) that GDM women with hypertension had significantly higher insulin resistance, positively correlated with MAP, insulin resistance than those with GDM alone. An increase in insulin existing in GDM women can contribute to vascular injury. Endothelial dysfunction caused by hyperinsulinemia, can be amplified by lipid abnormalities and activation of adrenal nervous system. All these factors are hypothesized to be involved in pathogenesis of hypertension in pregnancy. However, in our study no statistical differences in blood pressure and insulin resistance were found.

Interesting findings about GDM women were published by Oren et al. (1996). He studied diurnal arterial blood pressure profile among healthy pregnant women, as well as the women with GH and GDM. Although GDM group had normal blood pressure and physiological circadian pattern of BP was preserved, mass of heart's left ventricle was significantly greater than in normotensive group. Additionally, reduction in early diastolic filling was found. The author speculated that circulating factors such as glucose or insulin, may play a role. The observation may suggest that in GDM women not only metabolic symptoms of insulin resistance are present but also first signs of cardiovascular damage. That is why it is so important to treat the GDM women as a group of high risk of IRS with all its consequences. Treating GDM as an early phase of IRS enables to observe the natural history of IRS and to prevent the occurrence of the disease. Necessary lifestyle interventions, including weight loss, low-fat diet and moderate physical activity can reduce the risk of DM and cardiovascular diseases among the women.

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