ORIGINAL ARTICLE

# Maternal factors predictive of first-trimester pregnancy loss in women with pregestational diabetes

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**KEY WORDS**

diabetes, first trimester, miscarriage, pregnancy

**ABSTRACT**

**INTRODUCTION** Diabetes is one of the most frequent chronic diseases in women of childbearing age, which significantly increases the risk of complications at every stage of pregnancy.

**OBJECTIVES** The aim of the study was to investigate any maternal factors that may be associated with the risk of first-trimester pregnancy loss in patients with pregestational diabetes.

**PATIENTS AND METHODS** It was a retrospective study based on the data of 91 diabetic women in singleton pregnancy and with good perinatal outcome (74 women [81.3%] with type 1 and 17 [18.7%] with type 2 diabetes), and 60 diabetic women with a miscarriage (48 women [80%] with type 1 and 12 [20%] with type 2 diabetes). We analyzed selected maternal parameters at the first admission to the obstetrics department.

**RESULTS** Women in the miscarriage group were older compared with those in the good outcome group (29.5 ±5.4 years vs. 26.4 ±5.3 years; $P < 0.001$). Hemoglobin $A_{1c}$ ($HbA_{1c}$) was higher in the miscarriage group compared with the good outcome group (8.2% ±1.9% vs. 7.2% ±1.8%; $P < 0.001$). In a stepwise logistic regression analysis, maternal age at booking and $HbA_{1c}$ were found to be significant predictors of miscarriage (odds ratio [OR], 1.10; 95% confidence interval [CI], 1.02–1.18 and OR, 1.28; 95% CI, 1.026–1.61; respectively). A statistically insignificant trend towards first-trimester pregnancy loss was observed in patients with hypertension, overweight/obesity, unplanned pregnancy, longer duration of diabetes, and diabetic vascular complications.

**CONCLUSIONS** Suboptimal metabolic control and increasing maternal age are the most significant risk factors for first-trimester miscarriage in women with pregestational diabetes.

**INTRODUCTION** Pregestational diabetes complicates from 0.5% to 1% of all pregnancies.[1,2] It encompasses type 1 and type 2 diabetes as well as other rare types of diabetes. Despite a significant improvement in the access and quality of antenatal care, women with pregestational diabetes and their fetuses are at increased risk of serious complications compared with nondiabetic population. Many studies confirmed that pregestational diabetes significantly increases the risk of spontaneous abortion, preterm labor, hypertensive disorders, and operative deliveries.[3,4] An increased rate of congenital anomalies, growth disorders, stillbirths, birth trauma, metabolic alterations, and respiratory distress syndrome is commonly reported in the offspring born to diabetic mothers.[5-9] Maternal hyperglycemia remains the major and most widely studied factor altering fetal development, but other maternal factors might also adversely affect pregnancy outcome.[10] The complication of early pregnancy that is characteristic in women with pregestational diabetes is first-trimester pregnancy loss. Maternal hyperglycemia during the early stages of pregnancy seems to be the key modifiable factor contributing to this striking complication.[11] However, there are other known maternal risk factors that might increase this risk, such as advanced maternal age, previous spontaneous abortion, alcohol consumption, cigarette smoking, excessive maternal weight, and maternal diseases other than diabetes, particularly hypothyroidism, which is

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observed in up to 30% of the patients with type 1 diabetes.[12-17] These additional factors are significant in the general population. The vast majority of studies focused on comparing 2 different populations: pregnant diabetic women and healthy pregnant women. Considering that diabetes itself carries a risk for pregnancy, the comparison of these 2 groups for additional risk factors for miscarriage seems to be insufficient. Therefore, we designed a retrospective, observational study to test the hypothesis that early pregnancy loss in diabetic pregnancy is associated with the risk factors other than diabetes itself.

**PATIENTS AND METHODS** Data of 91 diabetic women (74 women [81.3%] with type 1 and 17 [18.7%] with type 2 diabetes) in singleton pregnancy and good perinatal outcome (delivering a healthy, mature newborn) and of 60 diabetic women (48 women [80%] with type 1 and 12 [20%] with type 2 diabetes) with a miscarriage (spontaneous pregnancy loss in the first trimester) were retrospectively retrieved from the database of the Department of Obstetrics and Women's Diseases, Poznan University of Medical Sciences, Poznań, Poland. The department is a tertiary reference center and provides care to pregnant diabetic women from the central-western Poland. All women were white Caucasians and conceived naturally. They were admitted to our department at least once before the 12th week of pregnancy according to the last menstrual period (LMP). Gestational age was confirmed with ultrasonographic measurement. The exclusion criteria for both groups were known disease other than diabetes and its complications that might increase the risk of miscarriage (known antiphospholipid syndrome or other thrombophilia, hypothyroidism), pregnancy following infertility treatment or assisted reproduction. Women with recurrent miscarriages (3 or more pregnancies that ended in miscarriage of the fetus before 20 weeks of gestation) were also excluded from the study.

Each pregnant woman with diabetes admitted to the department was thoroughly interviewed during the first antenatal visit (first trimester). If a woman was hospitalized more than once, the data concerning the course of pregnancy were further collected and stored in the database. First-trimester pregnancy loss was defined as expulsion of clinically confirmed intrauterine pregnancy, either spontaneous or medically induced after the diagnosis of a nonviable fetus (absent fetal heart rate) before 12 completed gestational weeks according to the last menstrual period and fetal crown rump length, if possible to measure. We used transvaginal ultrasound to confirm pregnancy. At the first antenatal visit, we recorded the following maternal parameters: maternal age, duration and type of diabetes, prepregnancy body mass index (BMI), concentration of hemoglobin $A_{1c}$ ($HbA_{1c}$), presence of vascular complications, hypertension, and pregnancy planning. Pregnancy was classified as planned if women attended counseling delivered by a diabetes specialist or by staff working at our specialist outpatient clinic for diabetes in pregnancy. Counseling took place before pregnancy and was aimed at achieving optimal metabolic control ($HbA_{1c}$ <6.1%), making necessary changes in pharmacotherapy (withdrawal of teratogenic drugs) and controlling chronic diabetic complications.

Severity of the disease was assessed according to the White classification for diabetic pregnancy. This classification expresses maternal risk during pregnancy and involves such parameters as duration of diabetes and the presence of vascular complications. We assessed patients for the following diabetic vascular complications: retinopathy, nephropathy, and ischemic heart disease. The diagnosis of retinopathy was based on a patient's history or data from fundoscopy performed in pregnancy. Similarly, the diagnosis of nephropathy was based either on a patient's report or protein loss in a 24-hour urine sample that exceeded 300 mg found throughout gestation. 24-hour urine sampling was routinely performed in every patient with pregestational diabetes admitted to our department.

In line with the Polish Gynecological Society standards of medical care in the management of women with diabetes, each woman with pregestational diabetes was admitted to our department as soon as the pregnancy was confirmed by her primary care gynecologist. Some patients were diagnosed with first-trimester intrauterine fetal death during first hospitalization in our department. In these patients, miscarriage was medically induced and it was their only hospitalization in our department. Some women from the miscarriage group were admitted to our department more than once during the first trimester. In those patients, viable pregnancy was diagnosed during the first hospital stay, and then they were admitted to the department second time with either inevitable, incomplete, or complete miscarriage and treated according to the protocol.

Statistical analyses were performed using MedCalc for Windows, version 12.1.3.0 (MedCalc Software, Mariakerke, Belgium). Testing for normal distribution was performed by the Kolmogorov-Smirnov test. The Mann-Whitney test was used to measure the significance of the difference between 2 independent samples. The $\chi^2$ or Fisher exact test was used for group comparison where appropriate. The Kruskal-Wallis test was used for comparing more than 2 independent samples. The receiver operating characteristic (ROC) curves were used to determine the cutoff values, sensitivity and specificity for chosen clinical parameters in the prediction of miscarriage. A logistic regression was used to analyze the relationship between 1 dichotomous dependent variable (pregnancy outcome) and independent variables (age at booking, duration of diabetes, prepregnancy BMI, $HbA_{1c}$ at booking). The levels of significance were indicated by *P* val-

ues. All *P* values of less than 0.05 were considered to indicate statistical significance.

All data analyzed were collected as part of routine diagnosis and treatment in the Department of Obstetrics and Women's Diseases. The study was based on a retrospective analysis of these data and does not require ethical approval.

**RESULTS** The characteristics of the study group are summarized in TABLE 1. Women who miscarried were significantly older than those with a good perinatal outcome (29.5 ±5.4 years vs. 26.4 ±5.3 years; *P* <0.001). A similar observation was reported for type 1 diabetic women compared separately between the miscarriage and the good outcome groups. Type 2 diabetic patients were older in the miscarriage group but the difference did not reach statistical significance. We observed a similar trend for diabetes duration: women from the miscarriage group had a longer history of the disease (11.9 ±8.6 vs. 9.4 ±6.5 years; *P* >0.05) but the difference was not statistically significant. The ROC curve analysis has shown the cutoff point of 27 years for the age at booking as the best predictor of miscarriage (sensitivity, 58.6%; specificity, 66.7%; area under the curve [AUC)], 0.67; *P* <0.001; FIGURE 1).

$HbA_{1c}$ at first antenatal hospitalization was significantly higher in women who lost their pregnancies (8.2% ±1.9% vs. 7.2% ±1.8%, *P* <0.001). The ROC curve analysis showed the cutoff point of 6.7% for $HbA_{1c}$ at booking as the best predictor of miscarriage (sensitivity, 81.1%; specificity, 49.7%; AUC, 0.67; *P* <0.001; FIGURE 2). $HbA_{1c}$

**TABLE 1** Characteristics of the study groups

| Variable | | Miscarriage group n = 60 | Good perinatal outcome group n = 91 | *P* |
|---|---|---|---|---|
| type 1 diabetic patients, n (%) | | 48 (80) | 74 (81.3) | >0.05[a] |
| type 2 diabetic patients, n (%) | | 12 (20) | 17 (18.7) | >0.05[a] |
| first hospital admission, gestational week | all patients | 7.8 ±2.2 | 8.4 ±2.3 | >0.05[b] |
| | type 1 diabetic | 8.0 ±2.2 | 8.2 ±2.3 | |
| | type 2 diabetic | 7.3 ±1.9 | 9 ±2.4 | |
| pregnancy loss, gestational week | all patients | 9.4 ±2.0 | – | – |
| | type 1 diabetic | 9.4 ±2.1 | – | |
| | type 2 diabetic | 9.1 ±1.8 | – | |
| age at booking, y | all patients | 29.5 ±5.4 | 26.4 ±5.3 | <0.001[b] |
| | type 1 diabetic | 28.2 ±4.5 | 25.1 ±3.6 | <0.001[b] |
| | type 2 diabetic | 35.5 ±5.1 | 31.9 ±4.5 | >0.05[b] |
| prepregnancy BMI, kg/m$^2$ | all patients | 24.4 ±5.8 | 23.7 ±5.9 | >0.05[b] |
| | type 1 diabetic | 22.5 ±3.7 | 22.4 ±3.0 | |
| | type 2 diabetic | 32.2 ±6.3 | 29.5 ±10.5 | |
| BMI at first hospitalization, kg/m$^2$ | all patients | 24.6 ±5.8 | 24.1 ±5.9 | >0.05[b] |
| | type 1 diabetic | 22.6 ±3.6 | 22.8 ±3.0 | |
| | type 2 diabetic | 32.5 ±6.2 | 29.9 ±10.6 | |
| duration of diabetes, y | all patients | 11.9 ±8.6 | 9.4 ±6.5 | >0.05[b] |
| | type 1 diabetic | 13.1 ±8.1 | 10.8 ±6.3 | |
| | type 2 diabetic | 7.1 ±6.8 | 3.4 ±2.9 | |
| $HbA_{1c}$ at booking, % | all patients | 8.2 ±1.9 | 7.2 ±1.8 | <0.001[b] |
| | type 1 diabetic | 8.5 ±2.0 | 7.4 ±1.9 | <0.001[b] |
| | type 2 diabetic | 7.0 ±1.1 | 6.2 ±0.9 | <0.05[b] |
| chronic hypertension, n (%) | all patients | 9 (15) | 7 (7.7) | >0.05[a] |
| | type 1 diabetic | 6 (12.5) | 2 (2.7) | 0.056[c] |
| | type 2 diabetic | 3 (25) | 5 (29.4) | >0.05[c] |
| presence of diabetic vascular complications, n (%) | all patients | 13 (21.7) | 18 (19.8) | >0.05[a] |
| | type 1 diabetic | 13 (27) | 18 (24.3) | >0.05[a] |
| | type 2 diabetic | – | – | – |
| pregnancy planning, n (%) | all patients | 15 (25) | 30 (33) | >0.05[a] |
| | type 1 diabetic | 11 (22.9) | 25 (33.8) | >0.05[a] |
| | type 2 diabetic | 4 (33.3) | 5 (29.4) | >0.05[c] |

Data are presented as mean ± standard deviation or number (percentage).

**a** $\chi^2$ test, **b** Mann-Whitney test, **c** Fisher's exact test

Abbreviations: BMI – body mass index, $HbA_{1c}$ – hemoglobin $A_{1c}$

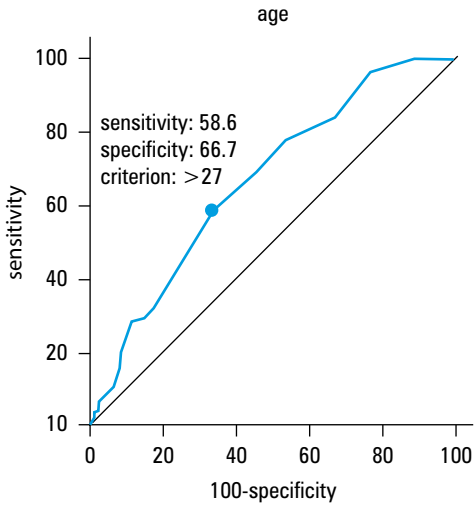


**FIGURE 1** Maternal age in the prognosis of miscarriage (area under the curve, 0.669; specificity, 66.7; sensitivity, 58.6; $P < 0.05$; cutoff point for maternal age, 27 years)

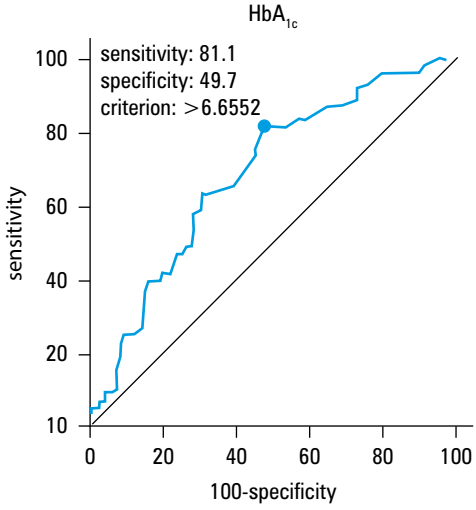


**FIGURE 2** Hemoglobin $A_{1c}$ in the prognosis of miscarriage (area under the curve, 0.674; specificity, 49.7; sensitivity, 81.1; $P < 0.05$; cutoff point for maternal $HbA_{1c}$, 6.7%)

levels according to pregnancy planning were different when comparing all groups together ($P < 0.001$) (TABLE 2), but also the subgroups. When we compared $HbA_{1c}$ within the miscarriage group, we found significantly higher $HbA_{1c}$ in the subgroup of patients who did not plan their pregnancies vs. patients who planned their pregnancies ($P < 0.001$). The same was observed when we compared $HbA_{1c}$ within the good outcome group, with significantly higher values in patients who did not plan their pregnancies ($P < 0.001$). The comparison of $HbA_{1c}$ in patients planning their pregnancies between the miscarriage and good outcome groups showed slightly higher values in patients from the miscarriage group; however, the difference was not statistically significant ($P = 0.07$). A similar comparison in patients who did not plan their pregnancies showed significantly higher $HbA_{1c}$ in patients from the miscarriage group ($P = 0.002$).

There was no difference in the mean prepregnancy BMI between the miscarriage and good perinatal outcome groups (24.4 ±5.8 kg/m² vs. 23.7 ±5.9 kg/m²; $P > 0.05$). However, although the proportion of overweight and obese patients was similar in both groups, we revealed a trend towards an increased number of overweight/obese women in the miscarriage group (31.7% vs. 24.2%; $P = 0.4$). We also found a trend for an increased number of patients with coexisting hypertension in the miscarriage group: 9 women who miscarried (15%) vs. 7 women who gave birth to healthy newborns (7.7%). However, this difference was nonsignificant ($P = 0.18$). Moreover, the difference was more pronounced when we compared type 1 diabetic patients separately, but it was of borderline significance ($P = 0.056$). We did not find any association between early pregnancy loss and chronic vascular complications because the number of patients with diabetic vascular disease was similar between the groups. The following conditions were diagnosed in 21.7% of the patients in the miscarriage group and 19.8% of those in the good outcome group: isolated nephropathy (n = 2 and n = 2, respectively), proliferative retinopathy (n = 4 and n = 11), or nephropathy and proliferative retinopathy (n = 7 and n = 5); classes F, R, and R/F according to the White classification, respectively. None of our patients had ischemic heart disease (class H according to White). We also did not note any episodes of ketoacidosis in our study group. None of the participants reported severe hypoglycemia (that would require an assistance of another person).

In a stepwise logistic regression analysis, independent variables such as maternal age at booking and $HbA_{1c}$ were found to be significant predictors of miscarriage (odds ratio [OR], 1.10; 95% confidence interval [CI], 1.02–1.18 and OR, 1.28; 95% CI, 1.026–1.61; respectively).

Types of antidiabetic therapies used before the first admission to our department in type 1 and type 2 diabetes are presented in TABLES 3 and 4.

**TABLE 2** Hemoglobin $A_{1c}$ in planned and unplanned pregnancies in the study groups

| | Miscarriage group | | Good perinatal outcome group | | *P* |
|---|---|---|---|---|---|
| | planned pregnancy, n = 13 (21.7%) | unplanned pregnancy, n = 47 (78.3%) | planned pregnancy, n = 30 (33%) | unplanned pregnancy, n = 61 (67%) | |
| $HbA_{1c}$ at booking, % | 6.5 ±0.8 | 8.7 ±1.8 | 6.0 ±0.8 | 7.7 ±1.8 | <0.001[a] |

Data are presented as mean ± standard deviation.

a Kruskal-Wallis test

Abbreviations: see TABLE 1

**TABLE 3** Type of therapy in type 1 diabetic patients before first admission

| Therapy | Miscarriage group n = 48 | Good perinatal outcome group n = 74 |
|---|---|---|
| intensive insulin therapy – human insulin, n (%) | 27 (56.3) | 45 (60.8) |
| mean $HbA_{1c}$, % | 8.8 | 7.5 |
| intensive insulin therapy – insulin analogs, n (%) | 16 (33.3) | 20 (27) |
| mean $HbA_{1c}$, % | 7.9 | 7.4 |
| premixed insulin, n (%) | 5 (10.4) | 9 (12.2) |
| mean $HbA_{1c}$, % | 9.1 | 7.0 |

Abbreviations: see **TABLE 1**

**TABLE 4** Type of therapy in type 2 diabetic patients before first admission

| Therapy | Miscarriage group n = 12 | Good perinatal outcome group n = 17 |
|---|---|---|
| diet, n (%) | 2 (16.7) | 8 (47.1) |
| mean $HbA_{1c}$, % | 6.9 | 5.9 |
| oral antidiabetic agents, n (%) | 4 (33.3) | 5 (29.4) |
| mean $HbA_{1c}$, % | 7.5 | 6.0 |
| oral antidiabetic agents + insulin, n (%) | 1 (8.3) | – |
| mean $HbA_{1c}$, % | 8.1 | – |
| insulin, n (%) | 5 (41.7) | 4 (23.5) |
| mean $HbA_{1c}$, % | 6.5 | 6.5 |

Abbreviations: see **TABLE 1**

**DISCUSSION** We confirmed that suboptimal maternal metabolic control still remains a significant risk factor for adverse perinatal outcome in diabetic population. Importantly, our data indicate that $HbA_{1c}$ often considered satisfactory for nonpregnant patients is not enough to reduce the risk to a background level. This is in agreement with the results of numerous studies which have shown that maternal hyperglycemia alters the development of pregnancy from the very beginning.[10,11,18,19] Nonetheless, a relatively low prognostic value of $HbA_{1c}$ at booking in the prediction of miscarriage (AUC, 0.67) confirms that it has a multifactorial background. Moreover, the additional analysis of $HbA_{1c}$ in relation to pregnancy planning indicated that women with a good peritoneal outcome who did not plan their pregnancies had higher $HbA_{1c}$ than those who had planned the pregnancy but experienced miscarriage. This finding further suggests that miscarriage in women with pregestational diabetes is the result of a complex interaction between the genetic and environmental factors.

We noted an increased risk for early pregnancy loss with $HbA_{1c}$ (6.7%, **FIGURE 2**) near to the level recommended for the young population with diabetes ($HbA_{1c}$<6.5%).[20] Nonetheless, it is important to mention that the goal of $HbA_{1c}$ below 6.5% is recommended in the population of patients who are not planning pregnancy/are not pregnant. Moreover, we found that patients from the miscarriage group who planned their pregnancies had the mean $HbA_{1c}$ level of 6.5%, which suggests insufficient control despite prepregnancy care. Our results confirm that only tight glycemic control as recommended by the Polish Diabetes Association ($HbA_{1c}$<6.1%), although rarely achieved in the general population, should be the goal of therapy for diabetic women of childbearing age.[20,21]

In our study, we also addressed the issue of an increasing maternal age. As the age of the childbearing population increases, maternal aging becomes an important background factor that also needs to be discussed with a diabetic patient. The ROC curve analysis showed a relatively weak association, but it is noteworthy that an increased risk of early pregnancy loss occurred in diabetic women well below the age of 35 years (**FIGURE 1**), which is considered to be associated with increased risk of fetal genetic abnormalities in the general population.

It is also well known that pregnancy planning in the population of diabetic women might reduce the risk of adverse pregnancy outcome including first-trimester miscarriage.[22,23] The majority of pregnancies in diabetic women are unplanned; therefore, active patient counseling should improve the proportion of diabetic women preparing for their pregnancies, thus decreasing the risk of an adverse pregnancy outcome.[24,25] Based on older and more recent data, pregnancy planning remains a challenge both for patients and for practitioners.[26,27] Our data increase the current knowledge by showing that in our region, only 29.8% of all participants received antenatal counseling. We also confirmed that pregnancy planning might reduce the risk of miscarriage in women with type 1 diabetes, although the difference was not statistically significant in the present study. The lack of statistical significance might be

caused by the fact that only a part of the patients who had planned their pregnancies achieved tight metabolic control. The number of patients who planned their pregnancies was similar among participants with type 2 diabetes (good perinatal outcome group vs. miscarriage group). However, these results need to be taken with caution due to a rather small group size. Nonetheless, there is no doubt that proper pregnancy planning helps reduce $HbA_{1c}$ levels, which has a favorable effect on pregnancy outcome. Therefore, it seems reasonable to include family planning issues to standard education programs for female teenagers and young women with diabetes and motivate them to maintain good metabolic control on a daily basis.

Of note, we did not find any association between diabetes duration and first-trimester miscarriages. Our results indicate that older age at booking is an independent risk factor for miscarriage and is unrelated to diabetes duration. We did not show a significant difference in the prepregnancy BMI between the groups. However, an insignificant trend for an increased number of overweight/obese women in the miscarriage group is clinically relevant because excessive weight gain is a commonly observed complication of insulin therapy.[28] Importantly, we confirmed that type 2 diabetic women in both groups had a relatively higher BMI compared with type 1 diabetic patients. Moreover, the prepregnancy BMI was the highest in type 2 diabetic women in the miscarriage group, which also had the highest share of patients on insulin. Our findings are in line with the results of other studies which have shown that an increased BMI predisposes to pregnancy loss.[29,30] In contrast, Maconochie et al.[12] reported that a low prepregnancy BMI might increase the risk of miscarriage. In the study conducted in women undergoing assisted reproduction techniques, Veleva et al.[31] showed that the relationship between the BMI and miscarriage is not linear but quadratic (U-shape), indicating a higher risk of miscarriage in both underweight and obese women.

All the above studies focus on nondiabetic populations and differ in their scope of analysis and factors studied. A recent study conducted by Persson et al.[32] in a large cohort confirmed both the increased prevalence of obesity in pregnant women with type 1 diabetes and the association between maternal obesity and fetal malformations, another early pregnancy complication characteristic for diabetic population. No data is available on any association between an increased maternal BMI and early pregnancy loss in women with pregestational diabetes. However, our results suggest that such a relationship might exist. Obesity itself, as a frequent component of metabolic syndrome, is a risk factor for the whole range of perinatal complications.[33] Therefore, women with diabetes should be particularly motivated to maintain their body weight within the reference values. Patients should be strongly advised and constantly educated to make the optimal use of dietary and lifestyle interventions instead of an increase in insulin doses. Chronic hypertension is a well-known risk factor for several pregnancy complications. Especially, when uncontrolled, it might predispose to preeclampsia, intrauterine growth restriction, intrauterine death, and placental abruption.[34] The presence of chronic hypertension in diabetic pregnant women might have additional negative effect on pregnancy outcome.[35] There is limited amount of data on the association between maternal hypertension and miscarriage. In a recent prospective observational cohort study, Moretti et al.[36] reported an increased risk of miscarriage (but not fetal malformation) in hypertensive pregnant women exposed to angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) in early gestation, compared with healthy controls and women with hypertension treated with another medications (18.0% vs. 8.9% vs. 11.8%, respectively).[36] In our study, we found no statistically significant difference in the occurrence of hypertension between the 2 analyzed groups. However, the proportion of patients with hypertension in the miscarriage group was higher than that in the good outcome group. In the view of the results presented by Moretti et al.,[36] this phenomenon might be the result of exposure to ACEI/ARB in some patients with hypertension who did not plan their pregnancy. Maternal hypertension is also associated with impaired placentation and improper remodeling of uterine arteries.[37,38] Thus, the coexistence of poor metabolic control, vascular disease associated with diabetes and that related to hypertension may have an additional negative effect on early embryonic and fetal development. Chronic vascular complications develop in a significant number of patients with long-lasting or poorly controlled diabetes. The presence of vascular complications put pregnant diabetic women at a higher risk of perinatal complications developing in the second half of pregnancy, such as preeclampsia, intrauterine growth restriction, and intrauterine death.[39,40] In our study, the presence of vascular complications was not significantly associated with an adverse outcome of early pregnancy. This observation, like the lack of association between early pregnancy loss and patient's diabetes duration, is of clinical importance. As new treatment strategies and therapies become more available, resulting in the overall improvement of metabolic control, we may expect an increased number of women with a long history of the disease and diabetic vascular disease willing to give birth. Such women can be reassured that, as long as they maintain good metabolic control, a long history of diabetes and even microvascular disease should not be considered as a risk factor for early pregnancy loss.

In conclusion, suboptimal maternal metabolic control and increasing maternal age remain the most significant risk factors for first-trimester

miscarriage in women with pregestational diabetes. A statistically insignificant trend towards first-trimester pregnancy loss was observed in patients with hypertension, overweight/obesity, unplanned pregnancy, longer duration of diabetes, and diabetic vascular complications, and these issues need to be addressed in preconception counseling for women with pregestational diabetes.

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ARTYKUŁ ORYGINALNY

# Czynniki ryzyka poronień w I trymestrze ciąży u kobiet z cukrzycą przedciążową

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**SŁOWA KLUCZOWE**

ciąża, cukrzyca, pierwszy trymestr ciąży, poronienie samoistne

**STRESZCZENIE**

**WPROWADZENIE** Cukrzyca jest jedną z najczęstszych chorób przewlekłych u kobiet w wieku rozrodczym, znacznie zwiększającą ryzyko powikłań na każdym etapie ciąży.

**CELE** Celem pracy była analiza czynników matczynych mogących mieć wpływ na ryzyko poronień w I trymestrze ciąży u pacjentek z cukrzycą przedciążową.

**PACJENCI I METODY** Retrospektywnej analizie poddano dane 91 pacjentek z cukrzycą w ciąży pojedynczej, z dobrym wynikiem położniczym, w tym 74 z cukrzycą typu 1 (81,3%) oraz 17 z cukrzycą typu 2 (18,7%) oraz dane 60 pacjentek z cukrzycą typu 1 (48; 80%) i typu 2 (12; 20%), które poroniły w I trymestrze ciąży. Analizie statystycznej poddano wybrane czynniki matczyne określone podczas pierwszej hospitalizacji na oddziale położniczym w I trymestrze ciąży.

**WYNIKI** Pacjentki, u których doszło do poronienia, były starsze od pacjentek z dobrym wynikiem położniczym (29,5 ±5,4 roku *vs* 26,4 ±5,3 roku; p <0,001). Odsetek hemoglobiny $A_{1c}$ ($HbA_{1c}$) był istotnie wyższy u pacjentek, które poroniły, niż u pacjentek z dobrym wynikiem położniczym (8,2 ±1,9% *vs* 7,2 ±1,8%, p <0,001). W analizie regresji logistycznej zarówno wiek matki, jak i odsetek $HbA_{1c}$ wykazały istotność statystyczną w predykcji poronień – odpowiednio OR 1,10 (95% CI: 1,02–1,18) oraz OR 1,28 (95% CI: 1,026–1,61). Podobny, choć nieistotny statystycznie trend w kierunku zwiększonego ryzyka poronień w tej grupie kobiet wykazano również dla nadciśnienia tętniczego, nadwagi/otyłości, nieplanowanej ciąży, dłuższego czasu trwania cukrzycy oraz powikłań naczyniowych cukrzycy.

**WNIOSKI** Niedostateczna kontrola metaboliczna cukrzycy i coraz starszy wiek matek są najistotniejszymi czynnikami ryzyka poronień w I trymestrze ciąży u kobiet z cukrzycą przedciążową.

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