

Maternal risk factors for neonatal acidosis in women with type 1 diabetes

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KEY WORDS

asphyxia, neonatal acidosis, pregestational diabetes, pregnancy, type 1 diabetes

ABSTRACT

INTRODUCTION Type 1 diabetes in the mother is associated with high risk of adverse neonatal outcomes. **OBJECTIVES** The aim of this study was to identify maternal factors associated with low arterial pH values (pH < 7.10) in infants of mothers with type 1 diabetes.

PATIENTS AND METHODS Data from 789 women were included in the analysis. Based on pH values in the umbilical arteries of infants, women were divided into 2 groups: those with normal pH, defined as pH of 7.1 or higher, and those with low pH, defined as pH lower than 7.1. A logistic regression analysis was used to identify the determinants of low pH in the umbilical artery, with data presented as odds ratios and 95% CIs.

RESULTS Low umbilical artery pH was observed in 72 infants (9.1%). There was an association between maternal glycated hemoglobin A_{1c} (HbA_{1c}) levels measured before delivery and low umbilical artery pH (odds ratio [OR] 1.40; 95% CI, 1.11–1.78; *P* = 0.01). A similar association was found for HbA_{1c} levels measured between 20 and 24 weeks' gestation (OR 1.29; 95% CI, 1.03–1.63; *P* = 0.03). There was no association between the levels of HbA_{1c} in the first trimester or lack of preconception care and low umbilical artery pH. In logistic regression, urgent cesarean section was associated with low umbilical artery pH (OR, 1.64; 95% CI, 1.11–2.44; *P* = 0.01), and this association was independent of HbA_{1c} levels measured before delivery.

CONCLUSIONS Lack of sufficient glycemic control in pregnancy is the strongest predictor of neonatal acidosis in women with type 1 diabetes.

INTRODUCTION Type 1 diabetes in the mother is associated with high risk of adverse neonatal outcomes. The most common complications are congenital malformations, premature delivery, fetal macrosomia, and birth injuries.^{1,2} In a study by Mimouni et al³, over 25% of infants delivered to diabetic women had perinatal asphyxia. Nowadays, due to significant improvements in diabetic and obstetric care, these numbers seem to have been reduced.⁴ Attempts should be made to prevent neonatal acidosis, because it is associated with a higher risk of postnatal adverse outcomes including neurological injuries, multiple organ dysfunctions, and increased long-term morbidity and mortality rates.^{5,6}

The analysis of umbilical artery pH values has been widely adopted in clinical practice. It is

especially recommended for high-risk populations such as pregnant women with diabetes. Some factors in the general population, such as prior cesarean delivery, maternal age of 35 years or older, previous neonatal death, general anesthesia, a thick meconium, uterine rupture, and abnormal fetal heart rate, have been identified as risk factors for neonatal acidosis.⁷ In women with type 1 diabetes, antepartum hyperglycemia correlates with umbilical erythropoietin levels at birth, which suggests that maternal hyperglycemia induces fetal hyperinsulinemia, hypoxemia, and, as a consequence, neonatal acidosis. However, there are limited data on the determinants of neonatal acidosis in pregnancy complicated by type 1 diabetes. We hypothesized that

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insufficient control of maternal diabetes might be a dominant factor predisposing to neonatal hypoxemia. Therefore, the aim of this study was to identify maternal factors associated with low cord arterial pH values in newborns of mothers with type 1 diabetes.

PATIENTS AND METHODS Clinical and laboratory data on 1069 women with type 1 diabetes and their infants for a period between 1993 and 2015 were extracted from the clinical registry of a tertiary care center of the Poznan University of Medical Sciences (Poznań, Poland). The hospital, including its outpatient clinic, is the biggest perinatal center for pregnant women with diabetes in Poland. It provides care for patients from the Wielkopolska Province (population of approximately 3.4 million people). A total of 280 women with diabetes were excluded from the analysis due to miscarriage (pregnancy loss before 22 weeks' gestation), major birth defects, multifetal pregnancy, diabetes other than type 1 or unspecified types, or incomplete information. Finally, data from 789 women with type 1 diabetes were included in the study. All women received intensive insulin therapy during pregnancy.

Registry of pregnant women with diabetes Clinical and laboratory data of women with type 1 diabetes have been collected and stored in our center continuously since 1993. According to the Polish Diabetes Association recommendations and our internal standards, every woman with preexisting type 1 diabetes from our region is immediately referred to our department once pregnancy is confirmed. Women with diabetes without complications have at least 3 planned, short-stay hospital admissions during pregnancy: in the first trimester, at midpregnancy (20–24 weeks' gestation), and near delivery (34–39 weeks' gestation). Patients who require more vigilant surveillance are admitted more frequently. Between hospital admissions, patients are referred for regular check-ups every 2 weeks at a hospital-based outpatient clinic.^{8,9} We recommend that all of our pregnant patients with type 1 diabetes deliver in our center. In this way, we have direct access to their pregnancy and peripartum data, including the umbilical cord blood gas analysis, which is routinely performed in our center.

Umbilical cord blood gas analysis For the purpose of this study, we analyzed pH values in the umbilical artery. Umbilical cord blood was collected separately from the artery and the vein, soon after birth, from a doubly clamped segment of the cord, and then immediately transported to the laboratory for analysis. During the sampling procedure, it is sometimes difficult to differentiate the artery from the vein, so we assumed that samples with lower pH came from the artery. Based on the pH values of the umbilical arteries of their infants, women were divided into 2 groups: normal pH,

defined as pH of 7.1 or higher, and low pH, defined as pH lower than 7.1.

Statistical analyses Statistical analyses were performed using the MedCalc software for Windows, version 12.1.3.0 (MedCalc Software, Mariakerke, Belgium). Testing for normality of data distribution was performed using the D'Agostino–Pearson test. The *t* test was used to measure the significance of the difference between 2 continuous variables when data fitted a normal distribution, with results presented as mean (SD). In the case of nonnormally distributed data, comparisons were made using the Mann–Whitney test, with results presented as the median and interquartile range. The χ^2 test was used for the comparison of categorical variables. A logistic regression analysis was used to identify the determinants of low pH in the umbilical artery, with data presented as odds ratios (ORs) and 95% CIs. Both the univariate and multivariate models were built to search for possible associations between variables. A 2-tailed *P* value of less than 0.05 was considered significant. The presence of vasculopathy was defined as being diagnosed with at least 1 of the following: retinopathy, nephropathy, or ischemic heart disease. Small for gestational age (SGA) was defined as a birth weight lower than the 10th percentile, and large for gestational age (LGA) was defined as a birth weight greater than the 90th percentile, using age- and sex-specific regional growth charts.

The degree of prematurity was described based on gestational age, and was divided into subgroups as follows: extremely preterm, less than 28 weeks' gestation; very preterm, 32 to 28 weeks' gestation; and moderate to late preterm, 32 to 37 weeks' gestation.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee as well as with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

This study is a retrospective analysis of routinely collected data and therefore is exempted from the formal review by the Poznan University of Medical Sciences Ethics Committee.

RESULTS The characteristics of the study subgroups are shown in [TABLE 1](#).

Among the study subgroups, there were no differences in maternal age, age at onset of diabetes, diabetes duration, the proportion of women receiving preconception care, the proportion of women with vasculopathy, gestational age at delivery, and body mass index (BMI).

A total of 72 infants (9.1%) had low pH in the umbilical artery. Low pH values were associated with a decreased Apgar score at 1 minute (OR, 0.76; 95% CI, 0.70–0.82; *P* < 0.001) and 5 minutes (OR, 0.77; 95% CI, 0.69–0.85; *P* < 0.001)

TABLE 1 Characteristics of women with type 1 diabetes divided into groups based on pH values in the umbilical arteries of their infants

Parameter	Normal pH (≥ 7.10) n = 717	Low pH (<7.10) n = 72	P value
Maternal age, y	28 (5)	28 (5)	0.7
Maternal age at diagnosis of type 1 diabetes, y	15 (8)	15 (9)	0.8
Diabetes duration, y	11 (7)	11 (8)	0.8
BMI, kg/m ²	23.2 (7.2)	23.9 (5.7)	0.2
HbA _{1c} , %	I trimester	7.3 (1.7)	0.08
	II trimester	6.1 (1.1)	0.02
	III trimester	6.3 (0.9)	<0.01
Pregnancy planning, n (%)	226 (31.5)	22 (30.5)	0.9
Vasculopathy, n (%)	189 (26.3)	22 (30.5)	0.5
Gestational age at delivery, wk	37 (2)	37 (3)	0.46
Birth weight, g	3298 (777)	3231 (853)	0.49

Data are presented as mean (SD) unless otherwise indicated.

Abbreviations: BMI, body mass index; HbA_{1c}, glycated hemoglobin A_{1c}

after birth. Maternal age (OR, 0.99; 95% CI, 0.94–1.04; $P = 0.72$), age at diagnosis of diabetes (OR, 1.01; 95% CI, 0.97–1.04; $P = 0.75$), and diabetes duration (OR, 0.99; 95% CI, 0.95–1.04; $P = 0.78$) were not associated with low umbilical artery pH. Maternal pre-pregnancy BMI (OR, 0.98; 95% CI, 0.94–1.02; $P = 0.4$), the presence of diabetic vascular complications (OR, 1.23; 95% CI, 0.73–2.01; $P = 0.44$), chronic hypertension (OR, 1.32; 95% CI, 0.65–2.70; $P = 0.44$), and gestational hypertension or preeclampsia (OR, 0.73; 95% CI, 0.32–1.65; $P = 0.44$) had no impact on low umbilical artery pH.

Low pH values were not associated with gestational age at delivery (OR, 0.95; 95% CI, 0.86–1.05; $P = 0.34$) or the degrees of prematurity, namely, late to moderate preterm (OR, 1.32; 95% CI, 0.76–2.31; $P = 0.33$), very preterm (OR, 1.55; 95% CI, 0.45–5.36; $P = 0.49$), and extremely preterm (there was only 1 extremely preterm infant with normal pH in the umbilical artery of 7.29). There was an association between maternal glycated hemoglobin (HbA_{1c}) levels measured before delivery and low pH in the umbilical artery (OR, 1.40; 95% CI, 1.11–1.78; $P < 0.01$). A similar association was found for HbA_{1c} levels measured between 20 and 24 weeks' gestation (OR, 1.29; 95% CI, 1.03–1.63; $P = 0.03$). There was no association between the first-trimester HbA_{1c} level as well as lack of preconception care and low pH in the umbilical artery. Predictors of low pH in the umbilical artery based on logistic regression models are shown in [TABLE 2](#).

Of the 107 newborns delivered via urgent cesarean section, 14 of them (13.1%) had low pH in the umbilical artery. There were 27 vacuum-assisted deliveries, and 3 of those newborns (11.1%) had low pH in the umbilical artery. There were 4 forceps deliveries, with low umbilical artery pH found in 2 newborns (50%). A logistic

regression revealed an association between the urgent cesarean section and low pH in the umbilical artery (OR, 1.64; 95% CI, 1.11–2.44; $P = 0.01$), and this association was independent of HbA_{1c} levels measured before delivery.

No association between either neonatal LGA or SGA and low pH in the umbilical artery was observed.

To address the possible influence of typical obstetric factors on umbilical artery pH values, we performed a separate analysis excluding urgent cesarean and operative vaginal deliveries. The association between HbA_{1c} levels measured between 20 to 24 weeks' gestation and before delivery remained significant (OR, 1.36; 95% CI, 1.04–1.77; $P = 0.02$ and OR, 1.41; 95% CI, 1.07–1.87; $P = 0.01$; respectively). Similarly, no association was found between the HbA_{1c} level in the first trimester and umbilical artery pH (OR, 1.16; 95% CI, 0.99–1.36; $P = 0.07$). There was still no association between low umbilical artery pH and maternal age, age at diagnosis of diabetes, diabetes duration, maternal prepregnancy BMI, the presence of diabetic vascular complications, chronic hypertension, gestational hypertension or preeclampsia, and neonatal LGA or SGA.

DISCUSSION This study is among the first to evaluate determinants of neonatal acidosis in women with type 1 diabetes in a cohort of this size.

In all women, we assessed multiple factors that might have potentially influenced neonatal acidosis. However, we demonstrated that only maternal levels of HbA_{1c} in the second and third trimesters of pregnancy and urgent cesarean sections were associated with low pH in the umbilical artery. In a population-based study of pregnant women with type 1 diabetes, Klemetti et al¹⁰ demonstrated an association between HbA_{1c} values measured closest to delivery and several adverse neonatal outcomes, including asphyxia, which is in line with our results. However, the authors did not find a relationship between HbA_{1c} levels measured in the first and second trimesters and neonatal asphyxia. In our study, there was also no association between the levels of HbA_{1c} in the first trimester and low pH in the umbilical artery. This might be explained by the fact that in general, patients' metabolic control was improved during pregnancy because of the intensification of treatment after admission to our center. Similarly, Striakov et al¹¹ revealed that in patients with preexisting diabetes mellitus, increased levels of HbA_{1c} during early pregnancy are not useful in predicting most adverse outcomes. Cahill et al¹² investigated the impact of glycemic control on neonatal morbidity in pregnancies complicated by gestational and pregestational diabetes and showed that the level of HbA_{1c} in late third trimester is the most useful predictor for neonatal risk in women with diabetes, which is in line with our findings. Cahill et al¹² focused mainly on Apgar scores of less than 7 at 5 minutes, but Locatelli et al⁵ demonstrated that, as expected, Apgar scores correlate with neonatal acidemia.

TABLE 2 Predictors of low pH in the umbilical artery based on logistic regression models

Predictors of low pH	Odds ratio (95% CI)	P value
HbA _{1c} II trimester ^a , %	1.29 (1.03–1.63)	0.02
HbA _{1c} III trimester ^a , %	1.40 (1.11–1.78)	0.03
Urgent cesarean section ^b , yes/no	1.64 (1.11–2.44)	0.01

a Univariate logistic regression

b Model adjusted for HbA_{1c} levels in the third trimester

Abbreviations: see TABLE 1

Elevated BMI predisposes women to numerous complications during pregnancy and labor. Cnattingius et al¹³ showed that a BMI value greater than 25 kg/m² in pregnant patients with diabetes is associated with an increased risk of low Apgar scores and severe asphyxia. In our study, we did not observe an association between maternal BMI and low pH value in the umbilical artery, but we focused only on pregnant women with type 1 diabetes, who are rarely obese or overweight.

Diabetic vasculopathy is a well-known risk factor for unfavorable pregnancy outcomes. Type 1 diabetic women with vasculopathy are at higher risk of preeclampsia and pathological fetal growth, as shown by Howarth et al.¹⁴ However, the authors did not investigate pH values in the umbilical artery. In our study, maternal vasculopathy was not associated with low pH in the umbilical artery. It may be explained by the fact that the majority of women with vasculopathy had elective cesarean delivery due to vasculopathy or other maternal indications.

It is essential that women with diabetes plan their pregnancies and achieve adequate metabolic control from the very beginning of pregnancy. Previous studies showed that patients with pregestational diabetes who plan their pregnancies achieve better obstetric outcomes.^{15,16} In our cohort, one-third of women attended preconception counseling, and these proportions were similar in groups with normal and low pH. This suggests that even in women with poorly controlled diabetes, intensification of treatment and normalization of glycemic control may have beneficial effects on the neonatal condition at birth.

Vascular complications of diabetes, such as nephropathy and retinopathy, are associated with longer duration of diabetes and with lack of adequate metabolic disease control. In 1949, White¹⁷ classified diabetes in pregnancy according to such factors as the age at onset of the disease, diabetes duration, and the presence of diabetic complications. Based on this classification, Klemetti et al¹⁸ investigated the pregnancy outcomes in women with type 1 diabetes. The authors found that the levels of HbA_{1c} in the first trimester, preeclampsia rates, cesarean delivery rates, deliveries before 37 weeks' gestation, and neonatal intensive care unit admissions increased from class B to F. It seems that the duration of diabetes can

influence these outcomes. In our study, the duration of diabetes or the presence of maternal vasculopathy were not associated with an increased risk of low pH in the umbilical artery.

Mialhe et al¹⁹ demonstrated that the HbA_{1c} level of 6.4% or higher at delivery was associated with urgent prelabor cesarean deliveries due to abnormal nonstress test results. Although the false-positive rate for the abnormal nonstress test is relatively high and can reach 55%, in numerous cases it can be a manifestation of varying degrees of fetal acidosis.²⁰ In our study, we used a direct method of evaluation of neonatal condition at birth, but our results seem to confirm the findings of Mialhe et al.¹⁹ Nonetheless, numerous urgent cesarean deliveries in our cohort could not be explained by maternal HbA_{1c} levels and were associated with typical obstetric indications.

Study limitations The study population included consecutive female patients with type 1 diabetes. These women were managed according to the same protocol in a single obstetric center for women with diabetes. However, because we collected data over a long period, we were not able to access all data concerning the delivery, such as the total duration and decision-to-delivery time in the cases of urgent cesarean and operative vaginal deliveries. Because all of these factors may influence umbilical artery pH, we conducted a subanalysis excluding women who delivered via urgent cesarean and operative vaginal procedures (vacuum, forceps). This left us with a subgroup of women who delivered vaginally or abdominally, with no signs of fetal distress. In this subgroup, the determinants of low umbilical artery pH remained unchanged. This suggests that the majority of women who delivered newborns with low umbilical artery pH did not present with any signs of fetal distress. This is an important clinical finding because fetal metabolic alterations, including acidosis, as an effect of maternal hyperglycemia may precede intrauterine fetal death.²¹⁻²³

Another limitation of the study is that our records included only early neonatal data, and we were not able to analyze long-term development of the neonates. Umbilical artery pH is an easily obtainable and useful parameter expressing neonatal asphyxia. However, it may not always correlate with the long-term neonatal development.

Conclusions Among modifiable risk factors, the lack of sufficient glycemic control in pregnancy is the strongest predictor of neonatal acidosis in women with type 1 diabetes. Therefore, improved glycemic control throughout pregnancy may reduce the risk of neonatal distress postpartum. However, a significant number of cesarean deliveries due to acute signs of fetal distress, resulting in low umbilical artery pH values in the infant, cannot be explained by maternal hyperglycemia, and these are probably related to classic obstetric factors.

ARTICLE INFORMATION

CONTRIBUTION STATEMENT PG and EW-O developed the project, collected or managed and analyzed data, and wrote and edited the manuscript. UM collected or managed and analyzed data. AZ collected or managed and analyzed data, and wrote and edited the manuscript. tA wrote and edited the manuscript. SL wrote and edited the manuscript.

CONFLICT OF INTEREST None declared.

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REFERENCES

- 1 Gunton JE, McElduff A, Sulway M, et al. Outcome of pregnancies complicated by pre-gestational diabetes mellitus. *Aust N Z J Obstet Gynaecol.* 2000; 40: 38-43. [↗](#)
- 2 Persson M, Norman M, Hanson U. Obstetric and perinatal outcomes in type 1 diabetic pregnancies: a large, population-based study. *Diabetes Care.* 2009; 32: 2005-2009. [↗](#)
- 3 Mimouni F, Miodovnik M, Siddiqi TA, et al. Perinatal asphyxia in infants of insulin-dependent diabetic mothers. *J Pediatr.* 1988; 113: 345-353. [↗](#)
- 4 Westerhuis ME, Schuit E, Kwee A, et al. Prediction of neonatal metabolic acidosis in women with a singleton term pregnancy in cephalic presentation. *Am J Perinatol.* 2012; 29: 167-174. [↗](#)
- 5 Locatelli A, Incerti M, Ghidini A, et al. Factors associated with umbilical artery acidemia in term infants with low Apgar scores at 5 min. *Eur J Obstet Gynecol Reprod Biol.* 2008; 139: 146-150. [↗](#)
- 6 Bobrow CS, Soothill PW. Causes and consequences of fetal acidosis. *Arch Dis Child Fetal Neonatal Ed.* 1999; 80: F246-F249. [↗](#)
- 7 Maisonneuve E, Audibert F, Guilbaud L, et al. Risk factors for severe neonatal acidosis. *Obstet Gynecol.* 2011; 118: 818-823. [↗](#)
- 8 Gutaj P, Wender-Ozegowska E, Brazert J. Maternal lipids associated with large-for-gestational-age birth weight in women with type 1 diabetes: results from a prospective single-center study. *Arch Med Sci.* 2017; 13: 753-759. [↗](#)
- 9 Gutaj P, Zawiejska A, Mantaj U, Wender-Ozegowska E. Determinants of preeclampsia in women with type 1 diabetes. *Acta Diabetol.* 2017; 54: 1115-1121. [↗](#)
- 10 Klemetti M, Nuutila M, Tikkanen M, et al. Trends in maternal BMI, glycaemic control and perinatal outcome among type 1 diabetic pregnant women in 1989-2008. *Diabetologia.* 2012; 55: 2327-2334. [↗](#)
- 11 Starikov RS, Inman K, Chien EK, et al. Can hemoglobin A1c in early pregnancy predict adverse pregnancy outcomes in diabetic patients? *J Diabetes Complications.* 2014; 28: 203-207. [↗](#)
- 12 Cahill AG, Tuuli MG, Colvin R, et al. Markers of glycemic control and neonatal morbidity in high-risk insulin-resistant pregnancies. *Am J Perinatol.* 2016; 33: 151-156.
- 13 Cnattingius S, Lindam A, Persson M. Risks of asphyxia-related neonatal complications in offspring of mothers with type 1 or type 2 diabetes: the impact of maternal overweight and obesity. *Diabetologia.* 2017; 60: 1244-1251. [↗](#)
- 14 Howarth C, Gazis A, James D. Associations of type 1 diabetes mellitus, maternal vascular disease and complications of pregnancy. *Diabet Med.* 2007; 24: 1229-1234. [↗](#)
- 15 Wender-Ozegowska E, Gutaj P, Szczepanek U, et al. Influence of pregnancy planning on obstetrical results in women with pregestational diabetes mellitus [in Polish]. *Ginek Pol.* 2010; 81: 762-767.
- 16 Tripathi A, Rankin J, Aarvold J, et al. Preconception counseling in women with diabetes: a population-based study in the North of England. *Diabetes Care.* 2010; 33: 586-588. [↗](#)
- 17 White P. Pregnancy complicating diabetes. *Pa Med J.* 1947; 50: 705-708.
- 18 Klemetti MM, Laivuori H, Tikkanen M, et al. White's classification and pregnancy outcome in women with type 1 diabetes: a population-based cohort study. *Diabetologia.* 2016; 59: 92-100. [↗](#)
- 19 Miall I, Le Ray C, Timsit J, Lepercq J. Factors associated with urgent cesarean delivery in women with type 1 diabetes mellitus. *Obstet Gynecol.* 2013; 121: 983-989. [↗](#)
- 20 Freeman RK, Anderson G, Dorchester W. A prospective multi-institutional study of antepartum fetal heart rate monitoring. I. Risk of perinatal mortality and morbidity according to antepartum fetal heart rate test results. *Am J Obstet Gynecol.* 1982; 143: 771-777. [↗](#)
- 21 Bradley RJ, Nicolaides KH, Brudenell JM, Campbell S. Early diagnosis of chronic fetal hypoxia in a diabetic pregnancy. *British Medical Journal (Clin Res Ed).* 1988; 296: 94-95. [↗](#)

22 Bradley RJ, Brudenell JM, Nicolaides KH. Fetal acidosis and hyperlactaemia diagnosed by cordocentesis in pregnancies complicated by maternal diabetes mellitus. *Diabet Med.* 1991; 8: 464-468. [↗](#)

23 Lauenborg J, Mathiesen E, Ovesen P, et al. Audit on stillbirths in women with pregestational type 1 diabetes. *Diabetes Care.* 2003; 26: 1385-1389. [↗](#)