DOI: https://doi.org/10.17816/JOWD58667

Pregnancy planning in women with diabetes mellitus type 2

© Natalya V. Borovik[1], Ekaterina V. Musina[2], Alyona V. Tiselko[1], Svetlana V. Suslova[2], Olga B. Glavnova[1], Maria I. Yarmolinskaya[1]

[1] The Research Institute of Obstetrics, Gynecology, and Reproductology named after D.O. Ott, Saint Petersburg, Russia;
[2] Maternity Hospital No. 6 named after Prof. V.F. Snegiryov, Saint Petersburg, Russia

BACKGROUND: The increase in the incidence of type 2 diabetes mellitus worldwide and the improvement in the quality of diabetic and obstetric care lead to an increase in the number of pregnant women with type 2 diabetes mellitus. The incidence of obstetric and perinatal adverse outcomes in women with type 2 diabetes mellitus is often higher than in women with type 1 diabetes. In the world literature, there are few works on the effect of pregnancy planning on the course and outcome of pregnancy in women with type 2 diabetes mellitus.

AIM: The aim of this study was to evaluate the role of pregnancy planning in patients with type 2 diabetes mellitus in improvement of pregnancy and birth outcomes.

MATERIALS AND METHODS: We retro- and prospectively analyzed the course and outcome of pregnancy in 124 women with type 2 diabetes mellitus, who were observed in the Diabetes Mellitus and Pregnancy Center of the Research Institute of Obstetrics, Gynecology and Reproductology named after D.O. Ott for the period from 2010 to 2019. The study included 34 women with type 2 diabetes mellitus at the stage of pregnancy planning and 90 women during pregnancy. All patients underwent a general clinical examination, carbohydrate metabolism correction, training at the School of Diabetes Mellitus in the principles of rational nutrition, self-control of glycemia and insulin therapy. Diabetes compensation was assessed by the level of glycated hemoglobin, determined using a method certified in accordance with the National Glycogemoglobin Standartization Program and standardized in accordance with the reference values adopted in the Diabetes Control and Complications Trial, as well as by the level of glycemia (self-control at least four times a day). We also assessed the severity of vascular complications of type 2 diabetes mellitus before and during pregnancy, and identified and treated comorbidities. To assess the degree of obesity, the criteria of the World Health Organization and the pregravid body mass index calculated by the Quetelet formula were used. The severity of preeclampsia was assessed in accordance with federal clinical guidelines. Ultrasound examination of the fetus with Doppler blood flow in the vessels of the fetoplacental complex was performed using a Voluson E6 ultrasound system (GE Healthcare, USA). For the timely diagnosis of diabetic fetopathy and fetal cardiomyopathy, dynamic fetometry and echocardiography were conducted. In addition, cardiotocography was performed for antenatal assessment of the fetus from the 30th week of pregnancy. After delivery, a neonatologist assessed the condition of the newborn using the Apgar scale at the first and fifth minutes of life, and then the assessment was carried out in the early neonatal period.

RESULTS: In the group of women who received pregravid training, the course and outcomes of pregnancy were significantly better: the frequency of preeclampsia was lower (14.7%) compared to the group of women with an unplanned pregnancy (40.0%); there was no severe preeclampsia compared to the same women (13.3%). The number of preterm births was significantly lower (14.7%) in the group of women with planned pregnancy compared to the group of women without pregravid preparation (37.8%). In addition, in the group of women planning pregnancy, there were no fetal congenital malformations, neonatal hypoglycemic conditions, hypertrophic cardiomyopathy; in the group of women with an unplanned pregnancy, these parameters being found to amount to 6.7%, 24.4% and 6.7%, respectively. There was no perinatal mortality in the group of women with a planned pregnancy; however, this parameter was shown to be 3.3% in the group of women with an unplanned pregnancy.

CONCLUSIONS: Pregnancy planning in patients with type 2 diabetes mellitus can significantly improve the course of pregnancy and childbirth outcomes.

Keywords: type 2 diabetes mellitus; pregnancy planning; pregnancy; obesity; preeclampsia; fetal macrosomia.

To cite this article:
Borovik NV, Musina EV, Tiselko AV, Suslova SV, Glavnova OB, Yarmolinskaya MI. Pregnancy planning in women with diabetes mellitus type 2. *Journal of Obstetrics and Women's Diseases.* 2021;70(3):11–19. DOI: https://doi.org/10.17816/JOWD58667

Received: 19.01.2021 **Accepted:** 10.03.2021 **Published:** 30.06.2021

УДК 618.3-06:616.379-008.64-07
DOI: https://doi.org/10.17816/JOWD58667

Влияние прегравидарной подготовки на течение и исход беременности у женщин с сахарным диабетом 2-го типа

© Н.В. Боровик[1], Е.В. Мусина[2], А.В. Тиселько[1], С.В. Суслова[2], О.Б. Главнова[1], М.И. Ярмолинская[1]

[1] Научно-исследовательский институт акушерства, гинекологии и репродуктологии им. Д.О. Отта, Санкт-Петербург, Россия;
[2] Родильный дом № 6 им. проф. В.Ф. Снегирева, Санкт-Петербург, Россия

Обоснование. Рост заболеваемости сахарным диабетом 2-го типа во всем мире, повышение качества оказания диабетологической и акушерской помощи приводят к увеличению количества беременных с сахарным диабетом 2-го типа. Частота акушерских и перинатальных неблагоприятных исходов у женщин с сахарным диабетом 2-го типа нередко выше, чем при сахарном диабете 1-го типа. В мировой литературе представлены немногочисленные работы по влиянию прегравидарной подготовки на течение и исход беременности у женщин с сахарным диабетом 2-го типа.

Цель — оценить эффективность прегравидарной подготовки у женщин с сахарным диабетом 2-го типа.

Материалы и методы. Были проанализированы (ретро- и проспективно) течение и исход беременности у 124 женщин с сахарным диабетом 2-го типа, наблюдавшихся в центре «Сахарный диабет и беременность» ФГБНУ «НИИ акушерства, гинекологии и репродуктологии им. Д.О. Отта» за период с 2010 по 2019 г. На этапе прегравидарной подготовки в исследование были включены 34 женщины с сахарным диабетом 2-го типа, во время беременности — 90 женщин. Всем пациенткам проводили общеклиническое обследование, коррекцию углеводного обмена, они проходили обучение в школе сахарного диабета — изучали принципы рационального питания, самоконтроля гликемии, инсулинотерапии. Компенсацию сахарного диабета оценивали по уровню гликированного гемоглобина, определенного с использованием метода, сертифицированного в соответствии с Национальной программой стандартизации гликогемоглобина (от англ. National Glycogemoglobin Standartization Program) и стандартизованного в соответствии с референсными значениями, принятыми в исследовании DCCT (от англ. Diabetes Control and Complications Trial), и по уровню гликемии (самоконтроль не реже четырех раз в сутки). Рассматривали также выраженность сосудистых осложнений сахарного диабета до и во время беременности, выявление и лечение сопутствующей патологии. Степень ожирения оценивали согласно критериям Всемирной организации здравоохранения и с учетом прегравидарного индекса массы тела, рассчитанного по формуле Кетле. Степень тяжести преэклампсии определяли в соответствии с федеральными клиническими рекомендациями. Ультразвуковое исследование плода с допплерометрией кровотока в сосудах фетоплацентарного комплекса выполняли при помощи аппарата Voluson E6 (GE Healthcare, США). Для своевременной диагностики диабетической фетопатии и кардиомиопатии плода проводили динамическую фетометрию и эхокардиографию. Для антенатальной оценки состояния плода с 30-й недели беременности выполняли кардиотокографию. После родоразрешения состояние новорожденного оценивал неонатолог по шкале Апгар на первой и пятой минутах жизни, затем наблюдали за течением раннего неонатального периода.

Результаты. В группе женщин, получивших прегравидарную подготовку, течение и исходы беременности были значительно лучше: частота преэклампсии была ниже (14,7 %) по сравнению с показателем в группе женщин с незапланированной беременностью (40 %), отсутствовала преэклампсия тяжелой степени (в группе женщин с незапланированной беременностью — 13,3 %). Количество преждевременных родов было достоверно ниже (14,7 %) в группе женщин с запланированной беременностью по сравнению с показателем в группе женщин с отсутствием прегравидарной подготовки (37,8 %). В группе планировавших беременность отсутствовали врожденные пороки развития плода, неонатальные гипогликемические состояния, гипертрофическая кардиомиопатия (в группе женщин с незапланированной беременностью эти показатели составили 6,7; 24,4; 6,7 % соответственно). Перинатальной смертности в группе женщин с запланированной беременностью не было, тогда как в группе женщин с незапланированной беременностью этот показатель составил 3,3 %.

Заключение. Прегравидарная подготовка у больных сахарным диабетом 2-го типа позволяет значительно улучшить течение беременности и исходы родов.

Ключевые слова: сахарный диабет 2-го типа; прегравидарная подготовка; беременность; ожирение; преэклампсия; макросомия.

Как цитировать:
Боровик Н.В., Мусина Е.В., Тиселько А.В., Суслова С.В., Главнова О.Б., Ярмолинская М.И. Влияние прегравидарной подготовки на течение и исход беременности у женщин с сахарным диабетом 2-го типа // Журнал акушерства и женских болезней. 2021. Т. 70. № 3. С. 11–19. DOI: https://doi.org/10.17816/JOWD58667

Рукопись получена: 19.01.2021 **Рукопись одобрена:** 10.03.2021 **Опубликована:** 30.06.2021

BACKGROUND

The increase in the incidence of type 2 diabetes mellitus (DM) over the past decades, improvement in the quality of the provision of diabetic and obstetric care, and use of assisted reproductive technologies lead to an increase in the number of pregnant women with type 2 DM. Worldwide, over the past 10–15 years, the number of pregnant women with type 2 DM has increased by 50%–90% [1–4]. The incidence of type 2 DM increases in parallel with the increase in the incidence of obesity. Over the past 20 years, the number of people who are overweight and obese has doubled globally. The prevalence of overweight and obesity in women of reproductive age has now reached 30%–35%, and by 2030, every second woman of reproductive age is predicted to be overweight. Over the past two decades, globally, the onset of type 2 DM has become noticeably younger. At this time, the incidence of type 2 DM in children and adolescents has increased several times in most countries. According to a national study conducted in the USA [5], the proportion of type 2 DM among DM types in young people aged 15–19 years varies from 5.5% to 80% and depends on the race, ethnicity, and region of residence. In Japan, more than 50% of all new reported cases of DM in young people age 10–19 years are type 2 DM [6].

According to the Diabetes Mellitus and Pregnancy Center of the D.O. Ott Research Institute of Obstetrics, Gynecology, and Reproductology, over the past 10 years, the number of pregnant women with type 2 DM has increased by 80%. The combination of type 2 DM and pregnancy poses a great threat to both the health of the mother and the development of the fetus and the condition of the newborn. Some studies [2, 7] have reported that the incidence of obstetric and perinatal adverse outcomes in women with type 2 DM is higher than in those with type 1 DM. Typically, patients with type 2 DM are obese, and they have hypertension and dyslipidemia, which aggravate the course and outcome of pregnancy in this female population. The development of all these diseases is based on insulin resistance. During late pregnancy, severe insulin resistance develops, which aggravates the course of DM. Many studies on planning pregnancy in women with type 1 DM have confirmed the efficiency of pregravid preparation (PP), but limited studied have provided data on planning pregnancy in women with type 2 DM.

PP in women with type 2 DM includes the following:

- Use of effective and safe contraceptives for the entire PP period.
- Informing the female patient about the possible risks of an adverse course and outcome of pregnancy (both for the mother and the fetus/newborn).
- Examination to clarify the state of carbohydrate metabolism and identification of DM complications, gynecological and somatic pathology, and their treatment.
- Teaching "DM and pregnancy" principles of disease management, rational nutrition, self-control, and insulin therapy techniques.
- Normalization of body weight (clinically significant weight loss by 10–15–20% depending on the initial body mass index for 3, 6, 9, and 12 months of PP).
- Achievement of target glycemic and glycated hemoglobin level during the antihyperglycemic therapy within 3–4 months before the intended conception; self-monitoring of blood glucose levels at least four times a day; when the individual optimal body weight is reached, oral antihyperglycemic drugs (prohibited for use during pregnancy in the Russian Federation) are discontinued, and insulin therapy is started if necessary.
- Cardiological examinations (such as electrocardiography, echocardiography, and blood pressure monitoring) to rule out coronary heart disease and adjust the antihypertensive therapy.
- Cessation of the use of angiotensin-converting enzyme inhibitors and selection of antihypertensive therapy (methyldopa and calcium channel antagonists) approved for use at the PP stage and during pregnancy when a significant decrease in body weight is achieved, as well as cessation of statins and fibrates due to their teratogenic effects.
- Prescription of folic acid preparations at a dose of 800–1000 μg/s 3 months before the intended conception to reduce the risk of diabetic embryopathy.
- If necessary, examination of the hemostasis system and correction of hyperhomocysteinemia.
- Correction of deficiency or insufficiency of vitamin D.
- Genetic counseling in the presence of a history of chromosomal pathology or congenital malformations (CM) of the fetus.
- Giving up smoking.

Upon reaching a clinically significant decrease in body weight, ideal compensation for DM and concomitant diseases, contraception is canceled. If pregnancy does not occur within a year, the couple is subjected to a thorough examination, and in the case of male infertility or tuboperitoneal factor, assisted reproductive technologies can be used.

This study aimed to assess the efficiency of PP in women with type 2 DM.

MATERIALS AND METHODS

The course and outcome of pregnancy of 124 women with type 2 DM, monitored at the Diabetes Mellitus and Pregnancy Center of the D.O. Ott Research Institute of Obstetrics, Gynecology, and Reproductology, from 2010 to 2019, were analyzed (retro- and prospectively). At the PP stage, 34 (27.4%) women presented to the center. Most of the patients in this group had a burdened obstetric history

(perinatal loss) or they planned to use assisted reproductive technologies. The rest of the participants (90) visited a specialized center during pregnancy (treatment period from 5 to 33 weeks), and the average treatment period was 21.0 ± 1.4 weeks.

The inclusion criteria were as follows:

- Type 2 pre-gestational DM
- Planning the pregnancy or having a progressive pregnancy

The exclusion criteria were as follows:

- Coronary artery disease
- Uncontrollable hypertension during antihypertensive therapy

All patients underwent a general clinical examination, adjustment of carbohydrate metabolism, and education on DM. DM compensation was assessed by the level of glycated hemoglobin determined using a method certified in accordance with the National Glycogemoglobin Standardization Program and standardized in accordance with the reference values adopted in the Diabetes Control and Complications Trial and by the level of glycemia (self-control at least four times a day). The severity of vascular complications of DM before and during pregnancy and detection and treatment of concomitant pathology were also assessed. To determine the degree of obesity, the criteria of the World Health Organization and the pregravid body mass index, calculated by the Quetelet formula, were used. The severity of preeclampsia was assessed in accordance with federal clinical guidelines [8]. Ultrasound examination of the fetus with Doppler examination of blood flow in the vessels of the fetoplacental complex was performed using a Voluson E6 apparatus (GE Healthcare, USA). For timely diagnostics of diabetic fetopathy and fetal cardiomyopathy, dynamic fetometry and echocardiography were performed. Starting from week 30 of pregnancy, cardiotocography was performed for the antenatal assessment of the fetus. After delivery, the condition of the newborn was assessed by the neonatologist using the Apgar scale at 1 and 5 min of life and then along the course of the early neonatal period. Data were statistically analyzed using parametric and nonparametric methods in Statistica software for Windows V. 8.0

RESULTS

A burdened obstetric history (such as non-developing pregnancies, spontaneous miscarriages, birth traumatism, and antenatal fetal death) was registered in 55% of women with PP and in 25% of women without PP. Table 1 presents the clinical characteristics of the patients examined. The groups were comparable in terms of age, DM duration, and presence of diabetic microvascular complications and arterial hypertension. More than 70% of the patients in both groups had obesity (70.5% in the PP group; 72.2% in the non-PP group). Given that all women in the PP group had reduced their pre-pregnancy weight by 6–27 kg (10–15–20% of the baseline); no morbid obesity was noted in this group.

Before the onset of pregnancy, all women who presented to the center for PP managed to achieve the target glycemic and glycated hemoglobin A1c values. Moreover, 70% of the women received oral hypoglycemic drugs (metformin, dipeptidyl peptidase-4 inhibitors, and liraglutide) before pregnancy, and the drugs were canceled before conception. From the planning stage, 10 (29.4%) women shifted to insulin therapy. In 65% of the patients from the group who presented to the center during pregnancy, the level of glycated hemoglobin A1c was >6.0%. When seeking specialized care during pregnancy, 35 (38.9%) women

Table 1. Clinical characteristics of the examined patients

Indicator	Planned pregnancies (*n* = 34)	Unplanned pregnancies (*n* = 90)
Average age, years	34.6 ± 0.8	34.0 ± 0.5
Duration of diabetes mellitus, years	3.0 ± 1.1	4.1 ± 0.1
HbA1c before pregnancy, %	**5.7 ± 0.1***	6.8 ± 0.1
Excessive body weight, *n* (%)	8 (23.5)	15 (16.7)
Degree I obesity, *n* (%)	10 (29.4)	20 (22.2)
Degree II obesity, *n* (%)	6 (17.6)	18 (20)
Degree III obesity, *n* (%)	**0***	12 (13.3)
Diabetic retinopathy, *n* (%)	2 (5.9)	7 (7.8)
Diabetic nephropathy, *n* (%)	1 (2.9)	4 (4.4)
Diabetic polyneuropathy, *n* (%)	3 (8.8)	9 (10)
Arterial hypertension, *n* (%)	9 (26.5)	23 (25.5)

* $p < 0.05$ when compared with the group of women who did not plan a pregnancy.

DOI: https://doi.org/10.17816/JOWD58667

received oral hypoglycemic drugs, namely, metformin, sulfonylureas, dipeptidyl peptidase-4 inhibitors, liraglutide, 6 (6.7%) received insulin therapy, and the rest (54.4%) received diet therapy only. In the PP group, 70% of them received bolus and basic-bolus insulin therapy during pregnancy, and 30% received diet therapy. In the non-PP group, 88% of the women shifted to insulin therapy during pregnancy, and the rest (12%) received diet therapy. Changes in the level of glycated hemoglobin A1c during pregnancy are presented in Figure.

In the PP group, the level of glycated hemoglobin A1c from the planning stage and throughout the pregnancy was below 6.0%. In trimester I of the non-PP group, only 35% of the patients had glycated hemoglobin A1c level lower than 6.0%, and the target values were achieved in 70% of the patients in trimester II and in 77% in trimester III.

Before pregnancy, more than 25% of the women in both groups had arterial hypertension (26.5% in the PP group and 25.5% in the non-PP group). At this stage, all women who presented to the center for PP were given drugs approved for use during pregnancy (such as methyldopa and calcium channel blockers). In the non-PP group, most of them (70%) did not receive antihypertensive therapy before pregnancy; 9 (10%) women took drugs contraindicated during pregnancy (such as angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and β-blockers). Poor DM compensation, vascular diabetic complications, and hypertensive disorders before pregnancy contribute to an increased incidence of preeclampsia, premature delivery, surgical delivery, and neonatal morbidity. The frequency of preeclampsia was significantly higher in the non-PP group at 40% than in the PP group at 14.7%. Fetoplacental insufficiency was detected in more than 20% of women (20.6% in the PP group, 24.4% in the non-PP group). The frequency of surgical delivery was higher in the PP group (70.6%) than in the non-PP group (57.8%). The course and outcome of pregnancy in the women examined are presented in Table 2.

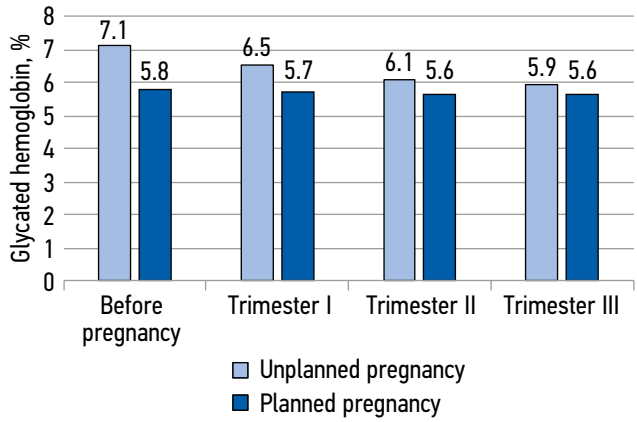

Figure. Dynamics of the level of glycated hemoglobin A1c during pregnancy

The most common indications for surgical delivery by cesarean section are as follows:

- Lack of effect from treatment and progression of the severity of preeclampsia (25%)
- Premature rupture of membranes in the absence of biological readiness for childbirth (20.2%)
- Scar on the uterus after cesarean section (20.2%)
- Fetal macrosomia (12.9%)
- Chronic placental insufficiency with hemodynamic disorders (11.3%)
- Onset of fetal hypoxia (8.1%)

In the PP group, 36 children (two twins) were born in a satisfactory condition (Apgar score at 1 and 5 min was ≥8 points). The average weight of the newborns was 3250 ± 121 g, macrosomia was detected in

Table 2. Course and outcome of pregnancy in the examined women with type 2 diabetes mellitus

Indicator	Planned pregnancies (*n* = 34)	Unplanned pregnancies (*n* = 90)
Moderate preeclampsia, *n* (%)	5 (14.7)*	24 (26.7)
Severe preeclampsia, *n* (%)	**0***	12 (13.3)
Delivery term, weeks	37.8 ± 0.1	37.0 ± 0.1
Preterm delivery, *n* (%)	5 (4.0)*	34 (37.8)
Cesarean section, *n* (%)	24 (70.6)	52 (57.8)
Newborn weight, g	3250 ± 121	3140 ± 72
Macrosomia, *n* (%)	4 (11.8)	25 (27.8)
Neonatal hypoglycemia, *n* (%)	**0***	22 (24.4)
Hypertrophic cardiomyopathy, *n* (%)	**0***	6 (6.7)
Congenital malformations of the fetus, *n* (%)	**0***	6 (6.7)
Perinatal mortality	**0***	3 (3.3)

* $p < 0.05$ when compared with the group of women who did not plan pregnancy.

4 (11.1%) children, and undernutrition was registered in 3 (8.3%) newborns. CM, hypertrophic cardiomyopathy, and neonatal hypoglycemic conditions were not recorded.

In the non-PP group, antenatal fetal deaths occurred in two cases (at 32/33 and 33/34 weeks of gestation, respectively); in one case, pregnancy was terminated at 24/25 weeks of gestation due to severe preeclampsia. Antenatal fetal death occurred in women who presented to a specialized center late (after week 30 of pregnancy) with unsatisfactory DM compensation (glycated hemoglobin level in trimester III was 6.7 ± 0.1%). The perinatal mortality rate in this group was 3.3%, and 88 children were born (1 twin); 56% of them were in satisfactory condition, 34% had mild asphyxia, and 10% had moderate and severe asphyxia. Fetal hypotrophy and macrosomia were detected in 10% and 27.8% of the cases, respectively. Macrosomia was assessed using the G.M. Dementieva centile tables in accordance with the height and weight indicators of gestational age (>75th percentile). Hypertensive disorders were registered in mothers who gave birth to low-birth-weight newborns. Neonatal hypoglycemic conditions were diagnosed on day 1 of life in 24.4% of the newborns. In this group, fetal CM and hypertrophic cardiomyopathy were detected in 6 (6.7%) newborns. Moreover, 12 (13.3%) newborns were transferred to other hospitals for further treatment and care.

DISCUSSION

Type 2 DM and obesity increase significantly the incidence of preeclampsia, surgical delivery, macrosomia, diabetic fetopathy, and neonatal intensive care provision [1, 9]. Pregnancy aggravated by pre-gestational DM is characterized by an increased incidence of hypertensive disorders and preeclampsia (15%–20%, which is three times higher than general population values) [10]. Risk factors include DM duration, arterial hypertension before pregnancy, severity of microvascular diabetic complications (especially diabetic nephropathy), and inadequate DM compensation. According to the literature, a direct correlation was found between the level of average daily glycemia in the first half of pregnancy and the severity of preeclampsia [11]. In our study, the incidence of preeclampsia was significantly lower in the PP group (14.7%) than in the non-PP group (40%). Severe preeclampsia was not detected in the PP group and reached the target glycemic and glycated hemoglobin level from the planning stage and during pregnancy, while this indicator was 13.3% in the non-PP group, which became the reason for the preterm delivery by cesarean section on an emergency basis.

Preterm delivery occurs in approximately one-third of pregnancies with pre-gestational DM [12]. Poor glycemic control and high HbA1c levels are significant risk factors for preterm delivery [13]. Indeed, it is confirmed by our data based on the high incidence of preterm delivery (37.8%) in the non-PP group compared with that in the PP group (4%). The incidence of surgical delivery by cesarean section was high in both groups with 50% (57.8% in the non-PP group and 70.6% in the PP group). The frequency of cesarean sections was higher in the PP group because 55% of the women had a burdened obstetric history (i.e., perinatal loss or uterine scar after cesarean section) compared with the non-PP group (25%).

A study reported that the perinatal mortality rate in type 2 DM ranged from 2.5% to 6.7% [13]. In our study, no perinatal mortality was registered in the PP group, while 3.3% perinatal mortality was recorded in the non-PP group. Diabetic fetopathy, which is mainly manifested by fetal macrosomia, as well as neonatal hypoglycemic conditions, and hypertrophic cardiomyopathy developed because of maternal hyperglycemia, which entails fetal hyperinsulinism. Fetal hyperinsulinemia results in increased body weight and in weight of some fetal organs (such as the liver, heart, and spleen) and retarded development of functional systems, homeostasis disorder, and impaired postnatal adaptation. In the literature [7, 14], macrosomia is registered in 30%–60% of children from mothers with DM and is a common cause of surgical deliveries, birth injuries, perinatal mortality, and neonatal morbidity. In the future, these children have an increased risk of obesity, DM, and arterial hypertension. In our study, the incidence of macrosomia was significantly lower in the PP group (11.8%) than in the non-PP group (27.8%). Neonatal hypoglycemic conditions were detected in 24.4% of children born to mothers with unplanned pregnancy. In the PP group, which was characterized by stable compensation of DM from the planning stage and during pregnancy, no neonatal hypoglycemic conditions were identified. The incidence of fetal CM in maternal pre-gestational DM reaches 6%–12% compared with population values of 2%–3% [15]. Up to 50% of all fetal CMs during pregnancy complicated by pre-gestational DM are malformations of the cardiovascular system, such as septal defects, transposition of the great vessels of the heart, and coarctation of the aorta. The incidence of inter-atrial septum defect and patent arterial duct increases with an increase in the mother's body mass index [16]. In our study, CMs were registered in 6 (6.7%) newborns in the non-PP group, including defects of the cardiovascular system (such as inter-atrial septum defect, interventricular septum defect, and coarctation of the aorta). Hypertrophic cardiomyopathy was detected in 6.7% of the newborns in the non-PP group; in one case, due to obstructive cardiomyopathy, the newborn was transferred to another hospital for intensive care. No CMs and cardiomyopathies were recorded in the PP group.

DOI: https://doi.org/10.17816/JOWD58667

CONCLUSIONS

The increase in the incidence of type 2 DM and obesity worldwide, advances in obstetric diabetology, and application of assisted reproductive technologies contribute to an increase in the number of pregnant women with pre-gestational DM. Until now, the incidence of fetal CM, miscarriage, preterm delivery, surgical delivery, perinatal mortality, and neonatal morbidity in DM remains high, exceeding the population level by more than two times. The results of the study showed that the course and outcomes of pregnancy in patients with type 2 DM, who received full-fledged PP, are much better and reach the general population values.

ADDITIONAL INFORMATION

Funding. The study was conducted within the budgetary funding of the institution.

Conflict of interest. The authors declare no conflict of interest.

Author contributions. *N.V. Borovik* created the study concept and design, wrote and edited the text, and provided final approval of the manuscript; *E.V. Musina* wrote and edited the text; *S.V. Suslova* collected the clinical material and edited the text, *O.B. Glavnova* collected the clinical material and processed and analyzed the data; *A.V. Tiselko* edited the text; *M.I. Yarmolinskaya* created the concept of the study, edited the text, and provided final approval of the manuscript. All authors made a significant contribution to the research and preparation of the article, read and approved the final version of the article before its publication.

REFERENCES

1. Kapur A, McIntyre HD, Hod M. Type 2 diabetes in pregnancy. *Endocrinol Metab Clin North Am.* 2019;48(3):511–531. DOI: 10.1016/j.ecl.2019.05.009

2. López-de-Andrés A, Perez-Farinos N, Hernández-Barrera V, et al. A population-based study of diabetes during pregnancy in Spain (2009–2015): Trends in incidence, obstetric interventions, and pregnancy outcomes. *J Clin Med.* 2020;9(2):582. DOI: 10.3390/jcm9020582

3. Mackin ST, Nelson SM, Kerssens JJ, et al. SDRN epidemiology group diabetes and pregnancy: national trends over a 15 year period. *Diabetologia.* 2018;61(5):1081–1088. DOI: 10.1007/s00125-017-4529-3

4. Fadl HE, Simmons D. Trends in diabetes in pregnancy in Sweden 1998–2012. *BMJ Open Diabetes Res Care.* 2016;4(1):e000221. DOI: 10.1136/bmjdrc-2016-000221

5. Caspard H, Jabbour S, Hammar N, et al. Recent trends in the prevalence of type 2 diabetes and the association with abdominal obesity lead to growing health disparities in the USA: An analysis of the NHANES surveys from 1999 to 2014. *Diabetes Obes Metab.* 2018;20(3):667–671. DOI: 10.1111/dom.13143

6. Funakoshi M, Azami Y, Matsumoto H, et al. Socioeconomic status and type 2 diabetes complications among young adult patients in Japan. *PLoS One*. 2017;12(4):e0176087. DOI: 10.1371/journal.pone.0176087

7. Murphy H, Steel S, Roland J, et al. Obstetric and perinatal outcomes in pregnancies complicated by Type 1 and Type 2 diabetes: influences of glycaemic control, obesity and social disadvantage. *Diabet Med.* 2011;28:1060–1067. DOI: 10.1111/j.1464-5491.2011.03333.x

8. Adamjan LV, Artymuk NV, Bashmakova NV, et al. Gipertenzivnye rasstrojstva vo vremja beremennosti, v rodah i poslerodovom periode. Prejeklampsija. Jeklampsija. Klinicheskie rekomendacii (protokol lechenija). Moscow; 2016. (In Russ.)

9. Gur'eva VM, Burumkulova FF, Petrukhin VA. Obstetric and perinatal outcomes in pregnant type 2 diabetic patients. *Almanac of Clinical Medicine*. 2015;(37):18–23. (In Russ.). DOI: 10.18786/2072-0505-2015-37-18-23

10. Murphy HR, Roland JM, Skinner TC, et al. Effectiveness of a regional prepregnancy care program in women with type 1 and type 2 diabetes: benefits beyond glycemic control. *Diabetes Care.* 2010;33:2514–2520. DOI: 10.2337/dc10-1113

11. Ajlamazjan JeK, Abashova EI, Arzhanova ON, et al. Saharnyj diabet i reproduktivnaya sistema zhenshchiny: rukovodstvo dlya vrachej. Moscow: GEOTAR-Media; 2017. (In Russ.)

12. Melamed N, Chen R, Soiberman U, et al. Spontaneous and indicated preterm delivery in pregestational diabetes mellitus: etiology and risk factors. *Arch Gynecol Obstet.* 2008;278(2):129–134. DOI: 10.1007/s00404-007-0541-z

13. Murphy HR, Bell R, Cartwright C, et al. Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nation wide study. *Diabetologia.* 2017;60(9):1668–1677. DOI: 10.1007/s00125-017-4314-3

14. Alexander LD, Tomlinson G, Feig DS. Predictors of large-for-gestational-age birthweight among pregnant women with type 1 and type 2 diabetes: A retrospective cohort study. *Can J Diabetes.* 2019;43(8):560–566. DOI: 10.1016/j.jcjd.2019.08.015

15. Ornoy A, Reece EA, Pavlinkova G, et al. Effect of maternal diabetes on the embryo, fetus, and children: congenital anomalies, genetic and epigenetic changes and developmental outcomes. *Birth Defects Res C Embryo Today*. 2015;105(1):53–72. DOI: 10.1002/bdrc.21090

16. Persson M, Razaz N, Edstedt Bonamy AK, et al. Maternal overweight and obesity and risk of congenital heart defects. *J Am Coll Cardiol*. 2019;73(1):44–53. DOI: 10.1016/j.jacc2018.10.050

СПИСОК ЛИТЕРАТУРЫ

1. Kapur A., McIntyre H.D., Hod M. Type 2 diabetes in pregnancy // Endocrinol. Metab. Clin. North. Am. 2019. Vol. 48. No. 3. P. 511–531. DOI: 10.1016/j.ecl.2019.05.009

2. López-de-Andrés A., Perez-Farinos N., Hernández-Barrera V. et al. A population-based study of diabetes during pregnancy in Spain (2009–2015): Trends in incidence, obstetric interventions,

and pregnancy outcomes // J. Clin. Med. 2020. Vol. 9. No. 2. P. 582. DOI: 10.3390/jcm9020582

3. Mackin S.T., Nelson S.M., Kerssens J.J. et al. SDRN epidemiology group diabetes and pregnancy: national trends over a 15 year period // Diabetologia. 2018. Vol. 61. No. 5. P. 1081–1088. DOI: 10.1007/s00125-017-4529-3

4. Fadl H.E., Simmons D. Trends in diabetes in pregnancy in Sweden 1998–2012 // BMJ Open Diabetes Res. Care. 2016. Vol. 4. No. 1. P. e000221. DOI: 10.1136/bmjdrc-2016-000221

5. Caspard H., Jabbour S., Hammar N. et al. Recent trends in the prevalence of type 2 diabetes and the association with abdominal obesity lead to growing health disparities in the USA: An analysis of the NHANES surveys from 1999 to 2014 // Diabetes Obes. Metab. 2018. Vol. 20. No. 3. P. 667–671. DOI: 10.1111/dom.13143

6. Funakoshi M., Azami Y., Matsumoto H. et al. Socioeconomic status and type 2 diabetes complications among young adult patients in Japan // PLoS One. 2017. Vol. 12. No. 4. P. e0176087. DOI: 10.1371/journal.pone.0176087

7. Murphy H., Steel S., Roland J. et al. Obstetric and perinatal outcomes in pregnancies complicated by Type 1 and Type 2 diabetes: influences of glycaemic control, obesity and social disadvantage // Diabet. Med. 2011. Vol. 28. P. 1060–1067. DOI: 10.1111/j.1464-5491.2011.03333.x

8. Адамян Л.В., Артымук Н.В., Башмакова Н.В. и др. Гипертензивные расстройства во время беременности, в родах и послеродовом периоде. Преэклампсия. Эклампсия. Клинические рекомендации (протокол лечения). Москва, 2016.

9. Гурьева В.М., Бурумкулова Ф.Ф., Петрухин В.А. и др. Акушерские и перинатальные исходы у беременных с сахарным диабетом 2-го типа // Альманах клинической медицины. 2015. № 37. С. 18–23. DOI: 10.18786/2072-0505-2015-37-18-23

10. Murphy H.R., Roland J.M., Skinner T.C. et al. Effectiveness of a regional prepregnancy care program in women with type 1 and type 2 diabetes: benefits beyond glycemic control // Diabetes Care. 2010. Vol. 33. P. 2514–2520. DOI: 10.2337/dc10-1113

11. Айламазян Э.К, Абашова Е.И., Аржанова О.Н. и др. Сахарный диабет и репродуктивная система женщины: руководство для врачей. Москва: ГЭОТАР-Медиа, 2017.

12. Melamed N., Chen R., Soiberman U. et al. Spontaneous and indicated preterm delivery in pregestational diabetes mellitus: etiology and risk factors // Arch. Gynecol. Obstet. 2008. Vol. 278. No. 2. P. 129–134. DOI: 10.1007/s00404-007-0541-z

13. Murphy H.R., Bell R., Cartwright C. et al. Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nationwide study // Diabetologia. 2017. Vol. 60. No. 9. P. 1668–1677. DOI: 10.1007/s00125-0174314-3

14. Alexander L.D., Tomlinson G., Feig D.S. Predictors of large-for-gestational-age birthweight among pregnant women with type 1 and type 2 diabetes: A retrospective cohort study // Can. J. Diabetes. 2019. Vol. 43. No. 8. P. 560–566. DOI: 10.1016/j.jcjd.2019.08.015

15. Ornoy A., Reece E.A., Pavlinkova G. et al. Effect of maternal diabetes on the embryo, fetus, and children: congenital anomalies, genetic and epigenetic changes and developmental outcomes // Birth. Defects. Res. C. Embryo. Today. 2015. Vol. 105. No. 1. P. 53–72. DOI: 10.1002/bdrc.21090

16. Persson M., Razaz N., Edstedt Bonamy A.K. et al. Maternal overweight and obesity and risk of congenital heart defects // J. Am. Coll. Cardiol. 2019. Vol. 73. No. 1. P. 44–53. DOI: 10.1016/j.jacc2018.10.050

AUTHORS INFO

Natalya V. Borovik, MD, Cand. Sci. (Med.);
ORCID: https://orcid.org/0000-0003-0835-6741;
eLibrary SPIN: 9010-7276;
e-mail: borovik1970@yandex.ru

Ekaterina V. Musina, MD, Cand. Sci. (Med.);
ORCID: https://orcid.org/0000-0002-7671-0637;
eLibrary SPIN: 6436-9293;
e-mail: e.musina@mail.ru

Alyona V. Tiselko, MD, Dr. Sci. (Med.);
ORCID: https://orcid.org/0000-0002-2512-833X;
eLibrary SPIN: 5644-9891;
e-mail: alenadoc@mail.ru

***Svetlana V. Suslova**, MD;
address: 3 Mendeleevskaya Line,
Saint Petersburg, 199034, Russia;
ORCID: https://orcid.org/0000-0001-7828-7250;
eLibrary SPIN: 8820-7250;
e-mail: sv07s@mail.ru

Olga B. Glavnova, MD;
ORCID: https://orcid.org/0000-0001-6087-252X;
eLibrary SPIN: 8040-5425;
e-mail: o.glavnova@mail.ru

ОБ АВТОРАХ

Наталья Викторовна Боровик, канд. мед. наук;
ORCID: https://orcid.org/0000-0003-0835-6741;
eLibrary SPIN: 9010-7276;
e-mail: borovik1970@yandex.ru

Екатерина Валентиновна Мусина, канд. мед. наук;
ORCID: https://orcid.org/0000-0002-7671-0637;
eLibrary SPIN: 6436-9293;
e-mail: e.musina@mail.ru

Алена Викторовна Тиселько, д-р мед. наук;
ORCID: https://orcid.org/0000-0002-2512-833X;
eLibrary SPIN: 5644-9891;
e-mail: alenadoc@mail.ru

***Светлана Валерьевна Суслова**;
адрес: Россия, 199034, Санкт-Петербург,
Менделеевская линия, д. 3;
ORCID: https://orcid.org/0000-0001-7828-7250;
eLibrary SPIN: 8820-7250;
e-mail: sv07s@mail.ru

Ольга Борисовна Главнова;
ORCID: https://orcid.org/0000-0001-6087-252X;
eLibrary SPIN: 8040-5425;
e-mail: o.glavnova@mail.ru

AUTHORS INFO

Maria I. Yarmolinskaya, MD, Dr. Sci. (Med.), Professor,
Professor of the Russian Academy of Sciences;
ORCID: https://orcid.org/0000-0002-6551-4147;
Researcher ID: P-2183-2014;
Scopus Author ID: 7801562649;
eLibrary SPIN: 3686-3605;
e-mail: m.yarmolinskaya@gmail.com

ОБ АВТОРАХ

Мария Игоревна Ярмолинская, д-р мед. наук,
профессор, профессор РАН;
ORCID: https://orcid.org/0000-0002-6551-4147;
Researcher ID: P-2183-2014;
Scopus Author ID: 7801562649;
eLibrary SPIN: 3686-3605;
e-mail: m.yarmolinskaya@gmail.com