

ZYGMUNY-SIEMBIDA, Ewelina, WRÓBLEWSKI, Hubert, ZIMNA, Aleksandra, WRÓBLEWSKA, Kinga, KOZDRA, Magdalena, PIASEK, Laura & OSIŃSKA, Aleksandra. The Gestational diabetes mellitus - pathogenesis, diagnosis, treatment and prognosis. *Quality in Sport*. 2023;11(1):11-15. eISSN 2450-3118. DOI <https://dx.doi.org/10.12775/QS.2023.11.01.001>
<https://apcz.umk.pl/QS/article/view/43203>

The journal has had 20 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32582. Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences). Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32582. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przynależność dyscypliny naukowej: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2023;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper. Received: 19.03.2023. Revised: 23.03.2023. Accepted: 08.04.2023. Published: 08.04.2023.

Gestational diabetes mellitus - pathogenesis, diagnosis, treatment and prognosis

- Ewelina Zygmunt-Siembida,¹
<https://orcid.org/0000-0002-3724-2164>
- ewelinazygmunt26@gmail.com
- Hubert Wróblewski,²
<https://orcid.org/0000-0002-1666-1650>;
hwwroblewski@gmail.com
- Aleksandra Zimna,²
<https://orcid.org/0000-0002-8712-3497>;
aleksandra_zimna97@wp.pl
- Kinga Wróblewska,³
<https://orcid.org/0000-0002-8740-9401>;
kinga.wroblewska.kw@gmail.com
- Magdalena Kozdra,⁴
<https://orcid.org/0009-0008-6109-4078>
magdakozdra5310@gmail.com
- Laura Piasek,²
<https://orcid.org/0009-0004-3104-3393>,
laurapiasek28@gmail.com
- Aleksandra Osinska,¹
<https://orcid.org/0009-0002-0351-9724>,
aleksandraosinska23@gmail.com

Correspondence: Ewelina Zygmunt-Siembida, ewelinazygmunt26@gmail.com

Abstract: Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy. It is characterized by hyperglycemia resulting from impaired tissue sensitivity to insulin secreted by pancreatic beta cells. This is due to the action of hormones secreted by the placenta that oppose insulin. The incidence of gestational diabetes continues to increase, posing many potential risks to both mother and fetus. Importantly, these complications also have a long-term dimension. It has been proven that in adulthood, in children born from pregnancies complicated by gestational diabetes, the risk of developing obesity, type II diabetes and cardiovascular diseases increases. Their mothers are also at a similar risk. The main goal of treatment of

¹ Military Clinical Hospital in Lublin, al. Raclawickie 23, 20-049 Lublin

² Samodzielny Publiczny Zakład Opieki Zdrowotnej MSWiA w Lublinie, Grenadierów 3, 20-331 Lublin

³ Student Research Group at Chair and Department of Epidemiology and Clinical Research Methodology, Medical University, Lublin

⁴ Medical University of Lublin, Aleje Raclawickie 1, 20-059 Lublin

gestational diabetes is to achieve normoglycaemia. Appropriate dietary management is recommended, and if this is not sufficient, insulin therapy should be initiated.

Key words: Gestational diabetes mellitus, insulin, hyperglycemia, diagnosis, pathophysiology, outcomes, dietary management,

Introduction

The term gestational diabetes was first used in 1961 by O'Sullivan. Gestational diabetes mellitus (GDM) is a carbohydrate metabolism disorder characterized by hyperglycemia that develops and is diagnosed during pregnancy.¹ Although it subsides after delivery, the consequences of this disease for both mother and baby can be long-lasting. Already at the stage of trying to get pregnant, we can identify women who are at increased risk of developing gestational diabetes. Risk factors for the development of gestational diabetes include:

- being overweight or obese,
- highly processed diet with a high glycemic index, poor in vitamins and minerals,
- positive history of gestational diabetes in a previous pregnancy,
- giving birth to a newborn weighing > 4000g,
- carbohydrate tolerance disorders diagnosed before pregnancy,
- glucosuria,
- advanced maternal age,
- diabetes mellitus in 1st and 2nd degree relatives.²

Women suffering from gestational diabetes, as well as children born from such a pregnancy, are burdened with an increased risk of developing obesity, type II diabetes and cardiovascular complications in the future. This leads to intergenerational transmission of predisposition to the development of metabolic diseases, which has a huge impact on the health of the entire population. Gestational diabetes most often develops in the second half of pregnancy. For this reason, according to current recommendations, every woman between 24 and 28 weeks of pregnancy should have a 75g oral glucose test (OGTT).³ An abnormal result of this test allows us to diagnose gestational diabetes. To minimize the possible consequences of this condition, both for the mother and the fetus, it is essential to maintain normal blood glucose levels. Treatment consists of implementing a diabetic diet and, if possible, increasing physical activity. In case of failure, insulin therapy is necessary. So far, oral antidiabetic drugs have not been approved for use in this indication.⁴

Pathogenesis of gestational diabetes mellitus

During a properly developing pregnancy, a number of physiological changes occur in a woman's body. Their task is to provide appropriate conditions for the developing fetus. One of them relates to the sensitivity of target tissues to insulin. At the beginning of pregnancy, tissue sensitivity to insulin increases. This is conducive to the creation of energy reserves for the later period of pregnancy. With the development of pregnancy, there is a physiological increase in the secretion of pregnancy hormones, such as estrogen, progesterone, placental lactogen or placental growth hormone. They are secreted mainly through the placenta, and their antagonistic effect on insulin leads to increasing insulin resistance of maternal tissues. The result of this mild state of maternal insulin resistance is an increase in endogenous hepatic glucose production as well as the breakdown of fat stores, leading to an increase in blood glucose and free fatty acids. As a result, more glucose needed for growth can pass through the placenta to the fetus. To keep maternal blood glucose levels stable, pancreatic beta cells begin to secrete even more insulin. Women with a disorder of this process may develop gestational diabetes.⁵

Dysfunction of the beta cells of the pancreatic islets in the course of gestational diabetes may result from several causes. Firstly, blood tests in some women with this diagnosis show circulating immune markers, such as anti-islet cell antibodies or antibodies to glutamate decarboxylase 65. They are diagnostic for developing type 1 diabetes. Some women have genetic variants that are diagnostic for monogenic forms of diabetes.⁶ These include genes responsible for subtypes of MODY diabetes and maternally inherited diabetes. However, the most common mechanism for the development of gestational diabetes is the presence of previous insulin resistance of tissues developing as a result of excessive body weight before pregnancy. Physiological processes occurring during pregnancy intensify this pathology even more, which leads to the breakdown of the beta cells of the pancreatic islets. This is why gestational diabetes is often seen as a form of developing type 2 diabetes.⁷

Diagnosis of gestational diabetes mellitus

Currently, the criteria of the International Association of Diabetes and Pregnancy Study Group (IADPSG) play a key role in the diagnosis of gestational diabetes (GDM). They are based on a large international study of 23,000 pregnant women - Hyperglycemia and Adverse Pregnancy Outcomes (HAPO).⁸ According to the recommendations of the IADPSG, every pregnant woman should have a fasting plasma glucose (FPG) test performed during her first visit to the gynecologist. Women with a normal result of this test (FPG < 92 mg/dl), not burdened with risk factors for hyperglycemia during pregnancy, should be ordered to perform a 75g oral glucose tolerance test (OGTT) between 24 and 28 weeks of pregnancy. Criteria for early OGTT testing include:

- fasting glucose of 92–125 mg/dL,
- pregnancy >35 years of age,
- previous birth of a child weighing > 4 kg or with a developmental defect,
- history of intrauterine death,
- hypertension or BMI > 27 kg/m² before pregnancy,
- family history of type 2 diabetes,
- previous gestational diabetes,
- multiple births.

Criteria for the diagnosis of gestational diabetes (according to WHO 2013) based on the OGTT with 75 g of glucose:

- 1) fasting blood glucose 5.1–6.9 mmol/L (92–125 mg/dL),
- 2) blood glucose in 1 h OGTT \geq 10 mmol/L (180 mg/dL),
- 3) blood glucose in 2 h OGTT 8.5–11.0 mmol/L (153–199 mg/dL).⁹

One of these criteria is sufficient to establish the diagnosis.

We also need to be aware that not only gestational diabetes can be diagnosed during pregnancy. Gestational diabetes is diagnosed when a woman meets the universal criteria for diabetes in the general population. Diagnosis criteria for diabetes in pregnancy (according to WHO 2013):

- 1) fasting blood glucose \geq 7.0 mmol/L (126 mg/dL) measured twice (on different days),
- 2) blood glucose at 2 hours 75 g OGTT \geq 11.1 mmol/L (200 mg/dL),
- 3) casual glucose \geq 11.1 mmol/L (200 mg/dL) and accompanying symptoms of hyperglycemia.¹⁰

Treatment of gestational diabetes mellitus

The basic treatment of gestational diabetes is a lifestyle change, consisting in the use of a proper diet and physical activity. The main goal of this procedure is to lower the elevated level of glucose in the mother's blood. This can be achieved by reducing the consumption of carbohydrates to less than 40% of the total energy value of food and by increasing the consumption of complex carbohydrates relative to simple ones. It is recommended that a woman eat regularly every 3–5 hours during the day. The recommended daily physical activity is 30 minutes of moderate-intensity aerobic exercise at least 5 days a week. Physical activity should be adapted to the woman's abilities.¹¹

Once GDM is diagnosed, close monitoring of blood glucose levels is necessary to ensure that adequate glycemic control is maintained. This is generally achieved through daily self-monitoring of blood glucose by patients using a glucometer. It is recommended to perform at least 4 measurements during the day - one measurement on an empty stomach, immediately after waking up, and three post-meal measurements - one hour or two hours after each main meal. Recommended blood glucose target is:

- fasting - 70-90 mg/dl,
- one hour after the start of the meal <140 mg/dl,
- two hour after the start of the meal <120 mg/dl.

The ACOG and ADA recommend the same threshold values for both gestational diabetes and pre-pregnancy diabetes.¹²

A woman should keep records of her glucose levels and what she ate. This allows her to see which foods trigger her glucose spikes. However, if lifestyle changes alone fail to achieve target values and most fasting and/or postprandial glucose levels are elevated, pharmacotherapy is recommended. Both the ACOG and the ADA recommend insulin for the drug treatment of GDM because it does not cross the placenta and improves perinatal outcomes.¹³ Insulin doses should be determined based on a careful analysis of the patient's blood glucose meter

readings. Fasting hyperglycemia is treated with basal (long-acting or intermediate-acting) insulin, and postprandial hyperglycemia is treated with mealtime (rapid-acting) insulin. Basal and meal insulin can be used separately or in combination, depending on the individual glycemic profile. Insulin dose modifications are made on the basis of self-monitoring of blood glucose under the strict supervision of a diabetologist. At present, oral treatment of GDM is controversial and data on long-term outcomes in offspring are lacking.¹⁴

Prognosis after gestational diabetes mellitus

Gestational diabetes adversely affects the health of both mother and baby. Unlike diabetes detected before or early in pregnancy, since GDM is most likely to develop in the second half of pregnancy, the risk of fetal malformations and miscarriage is low. In its course, the increase in placental transport of glucose, free fatty acids and amino acids to the fetus stimulates excessive endogenous production of insulin and insulin-like growth factor 1 (IGF-1). Both of these hormones have an anabolic effect, and the result of their excess is excessive fetal growth. This results in fetal macrosomia. Babies born from pregnancies complicated by GDM often weigh more than 4 kg, which increases the risk of shoulder dystocia during vaginal delivery. For this reason, fetal macrosomia is an indication for cesarean delivery.¹⁵ Despite the higher body weight, this does not mean that they are more developed than their peers. It is quite the opposite. Fetal hyperinsulinemia delays lung development. After birth, when there is a sudden interruption of glucose transported from the mother, the baby is at risk of hypoglycemia and electrolyte disturbances, such as hypokalemia. In addition, laboratory tests often reveal polycythemia and hyperbilirubinemia. The consequences of being born from a pregnancy complicated by gestational diabetes often follow the child throughout his life. It has been proven that they are at a much higher risk of developing obesity, type 2 diabetes and cardiovascular complications.¹⁶

Women with pregnancies complicated by GDM are at risk of developing hypertension and pre-eclampsia during pregnancy. All because of the negative impact of high glucose concentration on the invasion of the trophoblast, which impairs the function of the placenta. Due to fetal macrosomia, cesarean section is often necessary, as vaginal delivery poses a high risk of perineal damage.¹⁷ Women who have had gestational diabetes in a previous pregnancy are at risk of developing it again in a subsequent pregnancy. In addition, a diagnosis of GDM increases the risk of developing type 2 diabetes in the future by 20 times. These women are at greater risk of developing hypertension, myocardial infarction, stroke and further aggravation of metabolic disorders such as dyslipidemia.¹⁸

Conclusions

Gestational diabetes is undoubtedly one of the most common complications of pregnancy. The increasing percentage of overweight and obese women means that we will have to deal with this disease even more often. Screening for gestational diabetes should be performed in all pregnant women. Currently, a two-step strategy is recommended - measuring fasting blood glucose at the beginning of pregnancy and performing a three-point 75g oral glucose tolerance test (OGTT) between 24 and 28 weeks of pregnancy. The main goal of treating gestational diabetes is to keep a woman's blood glucose levels stable. The first-line treatment is lifestyle modification. However, every fourth woman requires pharmacotherapy. Insulin is the preferred first-line treatment. More research is needed on the efficacy and safety of oral diabetes medications. Fetal monitoring in the antenatal period usually begins at the end of the third trimester, and delivery is recommended between 39 + 0 and 39 + 6 weeks of gestation. If glycemic control is suboptimal, delivery should be considered between 37 + 0 and 38 + 6 weeks of gestation. Screening for impaired glucose tolerance and type 2 diabetes in the postpartum period is indicated for all women with a history of gestational diabetes, and further follow-up depends on the outcome of a 75 g oral glucose tolerance test performed between 4-12 weeks postpartum.

References

- ¹ Moreno-Castilla C., Hernández M., Bergua M., Alvarez M.C., Arce M.A., Rodriguez K., Martinez-Alonso M., Iglesias M., Mateu M., Santos M.D., et al. Low-Carbohydrate Diet for the Treatment of Gestational Diabetes Mellitus. *Diabetes Care*. 2013;36:2233–2238. doi: 10.2337/dc12-2714
- ² Durnwald C. Gestational diabetes: Linking epidemiology, excessive gestational weight gain, adverse pregnancy outcomes, and future metabolic syndrome. *Semin. Perinatol.* 2015;39:254–258. doi: 10.1053/j.semperi.2015.05.002.
- ³ Zhong C., Li X., Chen R., Zhou X., Liu C., Wu J., Xu S., Wang W., Xiao M., Xiong G., et al. Greater early and mid-pregnancy gestational weight gain are associated with increased risk of gestational diabetes mellitus. A prospective cohort study. *Clin. Nutr. ESPEN*. 2017;22:48–53. doi: 10.1016/j.clnesp.2017.08.013.
- ⁴ Camelo Castillo W., Boggess K., Stürmer T., Brookhart M.A., Benjamin D.K., Jonsson Funk M. Association of Adverse Pregnancy Outcomes with Glyburide vs Insulin in Women with Gestational Diabetes. *JAMA Pediatr*. 2015;169:452–458. doi: 10.1001/jamapediatrics.2015.74.
- ⁵ Di Cianni G., Miccoli R., Volpe L., Lencioni C., Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab. Res. Rev.* 2003;19:259–270. doi: 10.1002/dmrr.390.
- ⁶ Xiang AH, Peters RK, Trigo E, Kjos SL, Lee WP, Buchanan TA. Multiple metabolic defects during late pregnancy in women at high risk for type 2 diabetes mellitus. *Diabetes*. 1999;48:848–854
- ⁷ Buchanan TA, Xiang AH, Kjos SL, Watanabe RM. What is gestational diabetes? *Diabetes Care*. 2007;30(suppl 2):S105–S111.
- ⁸ International Association of Diabetes Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, et al. International Association of Diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33(3):676–82.
- ⁹ Egan A.M., Vellinga A., Harreiter J., Simmons D., Desoye G., Corcoy R., Adelantado J.M., Devlieger R., Assche A.V., Galjaard S., et al. Epidemiology of gestational diabetes mellitus according to IADPSG/WHO 2013 criteria among obese pregnant women in Europe. *Diabetologia*. 2017;1–9. doi: 10.1007/s00125-017-4353-9.
- ¹⁰ American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;37(Suppl. 1):S81–S90
- ¹¹ Viana LV, Gross JL, Azevedo MJ. Dietary intervention in patients with gestational diabetes mellitus: a systematic review and meta-analysis of randomized clinical trials on maternal and newborn outcomes. *Diabetes Care* 2014;37(12):3345–55
- ¹² American Diabetes Association. 14. Management of diabetes in pregnancy: standards of medical care in diabetes – 2020. *Diabetes Care* 2020;43(Suppl 1):S183–92
- ¹³ American Diabetes Association. Standards of medical care in diabetes - 2019. *Diabetes Care* 2019;42(Supplement 1):S1–193
- ¹⁴ Senat MV, Affres H, Letourneau A, et al. Effect of glyburide vs subcutaneous insulin on perinatal complications among women with gestational diabetes: a randomized clinical trial. *JAMA* 2018;319(17):1773–80.
- ¹⁵ Esakoff T.F., Cheng Y.W., Sparks T.N., Caughey A.B. The association between birthweight 4000 g or greater and perinatal outcomes in patients with and without gestational diabetes mellitus. *Am. J. Obstet. Gynecol.* 2009;200:672.e1–672.e4. doi: 10.1016/j.ajog.2009.02.035.
- ¹⁶ Vohr B.R., Boney C.M. Gestational diabetes: the forerunner for the development of maternal and childhood obesity and metabolic syndrome? *J. Matern. Fetal Neonatal Med.* 2008;21:149–157. doi: 10.1080/14767050801929430
- ¹⁷ National Institute for Health and Care Excellence. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period. NICE Guidelines NG3.2015. Last updated December 16, 2020
- ¹⁸ Xiang AH, Kjos SL, Takayanagi M, Trigo E, Buchanan TA. Detailed physiological characterization of the development of type 2 diabetes in Hispanic women with prior gestational diabetes mellitus. *Diabetes*. 2010;59:2625–2630.