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CURRENT STATUS OF GESTATIONAL DIABETES MELLITUS AND CLINICAL APPROACHES TO ITS MANAGEMENT

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Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy and is associated with an increased risk of adverse obstetric and perinatal outcomes. The study summarizes current data on the epidemiology, pathogenesis, diagnostic criteria, and screening approaches for GDM, as well as pregnancy management and postpartum follow-up for women with this disorder. Particular attention is paid to international clinical recommendations from IADPSG, ADA, ACOG, FIGO, and the World Health Organization, as well as controversial issues of universal and selective screening. The long-term metabolic consequences of GDM for the mother and fetus, in particular the risk of developing type 2 diabetes, were analyzed, and the clinical prospects for its prevention in women after GDM were considered.

Key words: gestational diabetes mellitus, pregnancy, insulin resistance, screening, perinatal complications.

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СУЧАСНИЙ СТАН ПРОБЛЕМИ ГЕСТАЦІЙНОГО ЦУКРОВОГО ДІАБЕТУ ТА КЛІНІЧНІ ПЕРСПЕКТИВИ ЇЇ ВИРІШЕННЯ

Гестаційний цукровий діабет (ГЦД) є одним із найпоширеніших метаболічних ускладнень вагітності та асоціюється з підвищеним ризиком несприятливих акушерських і перинатальних наслідків. У статті узагальнено сучасні дані щодо епідеміології, патогенезу, діагностичних критеріїв і підходів до скринінгу ГЦД, а також особливостей ведення вагітності та післяпологового спостереження жінок із цим порушенням. Особливу увагу приділено міжнародним клінічним рекомендаціям IADPSG, ADA, ACOG, FIGO та Всесвітньої організації охорони здоров'я, а також дискусійним питанням універсального й селективного скринінгу. Проаналізовано довгострокові метаболічні наслідки ГЦД для матері та плода, зокрема ризик розвитку цукрового діабету 2-го типу, і розглянуто клінічні перспективи його профілактики у жінок після перенесеного ГЦД.

Ключові слова: гестаційний цукровий діабет, вагітність, інсулінорезистентність, скринінг, перинатальні ускладнення.

The study is a fragment of the research project "Optimization of approaches to pregnancy management in women at high risk for the occurrence of obstetric and perinatal pathology", state registration No. 0122U201228.

Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance first detected during pregnancy that does not meet the criteria for overt diabetes [2, 4]. The increase in the incidence of GDM in recent decades has been associated with an increase in the average age of pregnant women, the prevalence of obesity, a sedentary lifestyle, increased stress levels, and revision of diagnostic criteria [1, 3]. The importance of the problem is due to both direct obstetric complications (development of preeclampsia, fetal macrosomia), an increase in the frequency of operative deliveries and neonatal complications, and an increased risk of developing type 2 diabetes in the mother. In addition, intrauterine hyperglycemia is considered a factor in programming metabolic disorders in children from a separate perspective [10, 12, 17, 31]. There are 2 classes of gestational diabetes: class A1 is controlled with diet, and class A2 requires drug treatment in addition to diet. Epidemiological studies report a GDM prevalence of 7–18 %, and in some populations it exceeds 20 % [1, 2, 30–32]. Despite significant progress in understanding the pathogenesis of GDM and improving its management, several issues remain controversial, including the choice of the optimal screening strategy and long-term follow-up of women after childbirth. In this regard, generalizing the current data is of practical importance for clinical work.

The purpose of the study was to summarize modern scientific concepts of gestational diabetes mellitus, its epidemiology, etiopathogenesis, diagnosis and screening, management of pregnancy with gestational diabetes mellitus, possible complications of pregnancy and childbirth, as well as to analyze the pathogenetic mechanisms of its impact on the condition of the fetus and newborn.

Materials and methods. A systematic review of the scientific literature was conducted to achieve the goal of the study, which involved a comprehensive summary of modern scientific data on etiopathogenesis, diagnostics and screening, pregnancy management in gestational diabetes mellitus, possible complications of pregnancy and childbirth, as well as an analysis of the pathogenetic mechanisms of its influence on the condition of the fetus and newborn.

We conducted an information search in the PubMed, Web of Science, Scopus, and Google Scholar databases. The list of references included publications from 2021–2026; sources published before 2021 were excluded, except for historically important information, which, if necessary, could be mentioned in the text. The analyzed sources included full-text original experimental studies and review articles in English and Ukrainian, published in peer-reviewed scientific journals. The search strategy involved the use

of the following terms and their combinations: gestational diabetes mellitus, pregnancy, insulin resistance, screening, perinatal complications.

The inclusion criteria were full-text peer-reviewed publications containing reliable experimental data on functional, biochemical, molecular, or morphological changes in the body of a pregnant woman and fetus under the influence of gestational diabetes mellitus.

As this work is a theoretical review based on publicly available scientific information, it did not require approval from a bioethics committee. We selected sources using the PRISMA approach. Initially, 274 publications were identified; after checking the bibliographic array, no duplicates were found, so we analyzed 274 records by title and abstract. Next, 72 full-text articles were assessed for eligibility criteria, and 30 were included in the final review.

Results of the study and their discussion.

Epidemiology. The prevalence of GDM varies significantly, from 5 % to 20 %, depending on the diagnostic criteria used and their popularity. The introduction of the IADPSG criteria significantly increased the frequency of GDM detection, which, on the one hand, enabled the identification of women with moderate hyperglycemia and, on the other hand, sparked discussions about the feasibility of universal screening [2, 4]. However, the introduction of IADPSG criteria is considered a possibility for early prevention of pregnancy complications [9]. The main risk factors for the development of GDM include maternal age over 35 years, overweight or obesity (BMI>30), pathological weight gain in the 1st-2nd trimester of pregnancy, a strong family history of diabetes, GDM in previous pregnancies, polycystic ovary syndrome, physical inactivity, smoking, chronic stress (especially wartime stress), hypertension, long-term use of glucocorticosteroids, birth of a child from a previous pregnancy with a body weight ≥ 4000 grams, ante-/intranatal death of the fetus or newborn of unknown cause [1, 3].

Etiopathogenesis of diabetes mellitus. The pancreas's endocrine function is to maintain a stable blood glucose level. The endocrine part of the pancreas is represented by the islets of Langerhans-Sobolev, which are located throughout the gland, but most of them are in the tail. The total weight of the endocrine part of the pancreas is approximately 3 grams. Islet cells are composed of several types of cells: β -, α -, and Δ -cells, which produce insulin, glucagon, and somatostatin, respectively.

Insulin affects all types of metabolism because it is an anabolic hormone that promotes glucose utilization and the biosynthesis of glycogen, lipids, and proteins. In insulin deficiency, tissues absorb glucose poorly, gluconeogenesis increases, hyperglycemia occurs, and all types of metabolism are disrupted, causing damage to blood vessels, nerves, and many other tissues.

Under glucagon's influence, the liver produces glucose by stimulating glycogen breakdown (glycogenolysis).

Somatostatin inhibits the secretion of glucagon, insulin, and other hormones. Prolonged exposure to high doses of somatostatin is accompanied by the

development of insulin resistance in muscle and adipose tissue.

Pregnancy is a diabetogenic state because, during gestation, the energy needs of the fetus are provided by the mother's glucose; there is an increase in glucose utilization by the fetus and inhibition of gluconeogenesis, which leads to moderate hypoglycemia in the pregnant woman on an empty stomach; glucose freely penetrates through the placenta to the fetus by facilitated diffusion due to the concentration gradient. These factors cause hypoglycemia in pregnant women with decreased blood insulin levels; however, after eating, glycemia increases not because of insulin deficiency, but because of insulin resistance (due to the counterinsular action of placental hormones).

During physiological pregnancy, carbohydrate metabolism changes to meet the fetus's high energy needs (mainly glucose). In the first trimester, blood glucose levels decrease and tissue sensitivity to insulin increases, reflecting the fetus's growing glucose demand and potentially leading to hypoglycemia. From the 13th week of pregnancy, with any diabetes, the pregnant woman experiences a worsening of the course of the disease: hyperglycemia increases, which can lead to ketoacidosis; the need for insulin increases due to the counterinsular effect of placental hormones. From the 32nd week of pregnancy until delivery, the course of diabetes may improve again, which is associated with increased consumption of glucose by the fetus, which enters it through the placenta from the mother's blood; during childbirth, there is a significant fluctuation in blood glucose levels, and hyperglycemia and acidosis may develop under the influence of emotional factors (pain, fear) or hypoglycemia as a result of physical work. After childbirth, blood glucose decreases briefly, then gradually increases, reaching the level the woman had before pregnancy by the 7th day of the postpartum period.

Diabetes mellitus is a disease characterized by chronic hyperglycemia caused by an absolute deficiency of insulin (when the pancreas produces little of the hormone; type I diabetes mellitus) or by a relative deficiency (when tissues are less sensitive to insulin). However, the pancreas's secretory function is not impaired (type II diabetes mellitus). Pregnant women may develop transient impaired glucose tolerance, which disappears after the pregnancy ends (gestational diabetes mellitus).

The pathogenesis of gestational diabetes mellitus results from a combination of pregnancy-related physiological insulin resistance and relative insufficiency of insulin secretion by pancreatic β -cells. In the second half of pregnancy, under the influence of placental hormones – placental lactogenesis, progesterone, estrogens, cortisol – there is a decrease in the sensitivity of the pregnant woman's peripheral tissues to insulin, which contributes to providing the fetus with glucose [3, 5, 6, 11]. As a result of this relative insulin resistance, healthy pregnant women experience a compensatory increase in insulin secretion, which allows them to

maintain normoglycemia. Chronic inflammation, adipokine imbalance, and epigenetic mechanisms associated with obesity play an important role in this [2, 6, 13, 24, 25]. Maternal hyperglycemia causes fetal hyperinsulinemia, which is a key link in the formation of macrosomia and fetopathy, impaired adaptation of the newborn, and metabolic programming of obesity in later life.

Diagnostics and screening. The optimal screening strategy for GDM remains a subject of active debate. Today, various professional communities recommend one- and two-stage approaches to diagnosis. According to IADPSG and WHO recommendations, a one-stage approach uses a 2-hour oral glucose tolerance test (OGTT) with a 75 g glucose load at 24–28 weeks of pregnancy, because the counterinsular effect of placental hormones is maximally expressed at this time.

The diagnosis of GDM or overt diabetes mellitus is established in the presence of at least one pathological glycemic index [1, 2, 4].

This test is performed in the morning after an 8-hour fast, provided that there is no corticosteroid use, acute illness, injury, or surgery. Glycemia is determined in venous blood plasma by a laboratory method (not with the help of an expert analyzer). After blood sampling on an empty stomach, the pregnant woman is given 75 g of glucose dissolved in 300 ml of still water to drink over 3–5 minutes (fresh lemon juice can be added). Blood samples are taken again at 1 and 2 hours (during this period, you cannot eat, but you can drink unsweetened water). The test is considered positive if at least one indicator – fasting and/or post-exercise glycemia – meets the given diagnostic criteria (Table 1).

Table 1

Results of oral glucose tolerance test in pregnant women

Glycemic profile status	Fasting plasma glucose level (mmol/L)	Plasma glucose level 1 hour after loading (mmol/L)	Plasma glucose level 2 hours after loading (mmol/L)
Normal	<5.1 mmol/L	<10.0 mmol/L	<8.5 mmol/L
Gestational diabetes mellitus	5.1-6.9 mmol/L	10.0-11.0 mmol/L	8.5-11.0 mmol/L
Manifest DM first detected	≥7.0 mmol/L	≥11.1 mmol/L	≥11.1 mmol/L

Pregnancy management for gestational diabetes. The basis of GDM treatment is lifestyle modification, which includes individualized diet therapy and dosed physical activity. Nutrition should be balanced in calories, with restricted, easily digestible carbohydrates and evenly distributed meals throughout the day [3]. Self-monitoring of blood glucose is an essential component of the management of pregnant women with GDM. If non-drug measures are ineffective within 1–2 weeks, insulin therapy is indicated as the method of choice [4, 5, 18, 19]. If serum creatinine is elevated, the albumin-to-creatinine ratio exceeds 30 mg/mmol, or total protein excretion exceeds 2 g/day, refer the woman to a nephrologist. To prevent preeclampsia, pregnant women at risk are prescribed acetylsalicylic acid 100–150 mg/day and calcium 2 g/day. To detect congenital malformations, women with diabetes are prescribed an ultrasound to detect structural abnormalities in the fetus, including examination of the fetal heart (4 chambers, presence of outflow tracts, and 3 umbilical vessels), at 2 weeks. Monitoring fetal growth and well-being is mandatory for pregnant women with any form of diabetes. Ultrasound monitoring of fetal growth and amniotic fluid is performed every 4 weeks from 28 to 36 weeks. It is necessary to provide an individualized approach to monitoring fetal growth and well-being in women with diabetes and at risk of fetal growth retardation [2, 7, 11, 17].

The threat of preterm birth in women with diabetes is not a contraindication to antenatal steroid prophylaxis for fetal lung maturation or tocolysis. However, women with diabetes who are treated with insulin and receive steroids for fetal lung maturation should be given additional insulin according to an agreed protocol and have their blood glucose levels closely monitored.

The use of oral hypoglycemic drugs during pregnancy remains limited and requires an individualized approach. Metformin and glibenclamide are not recommended as first-line therapy because both drugs cross the placental barrier.

Pregnant women with pre-existing diabetes should have a retinal assessment using digital imaging and tropicamide dilation after their first antenatal clinic visit (if a retinal assessment has not been performed within the past 3 months) and again at 28 weeks.

If renal function has not been assessed within the previous 3 months in women with pre-existing diabetes, such an assessment should be performed at the woman's first visit to the doctor during pregnancy.

If serum creatinine is elevated, the protein-to-creatinine ratio is greater than 30 mg/mmol, or total protein excretion exceeds 2 g/day, the woman should be referred to a nephrologist [2, 7, 25, 29].

Childbirth. Carrying a pregnancy to term is permissible provided that it is uncomplicated and there are no signs of fetal distress. Most clinicians recommend delivery between 36 and 38 weeks of gestation. The choice of delivery method depends on the course of diabetes, the condition of the mother and fetus, and fetal size.

Delivery through the natural birth canal is the best option. Still, it is necessary to take into account the size of the woman's pelvis and the weight of the fetus (clinical discrepancy may occur), as well as the possibility of significant injuries to the birth canal of the mother and fetus (clavicle fractures, intra-abdominal injuries).

Childbirth should be conducted in the presence of an endocrinologist, with adequate anesthesia, correction of labor activity in case of weakness of labor forces; do not force the removal of the shoulders; carry out

prevention of bleeding in the third and early postpartum periods; prevention of postpartum infectious diseases, lactational mastitis, and hypogalactia.

Indications for elective cesarean section: "fresh" retinal hemorrhages; severe preeclampsia; predisposition to ketoacidosis; increasing signs of diabetic nephropathy; fetal distress; breech presentation of the fetus; fetal weight > 4000 g [7, 12, 17, 24].

Possible complications of pregnancy and childbirth with GDM:

- during pregnancy: premature abortion (occurs in 15–30 %), preeclampsia (30–50 % of cases), polyhydramnios (20–30 %), inflammatory diseases of the urinary tract (up to 16 %), placental dysfunction, increased risk of obesity and arterial hyperplasia;

- on the part of the fetus: developmental anomalies (8 %), large and giant fetus, fetal distress, its antenatal death (24 %), high level of early infant mortality (up to 10 %);

- complications in childbirth: premature rupture of membranes, weak labor activity, clinically narrow pelvis, birth canal injuries, fetal distress, obstetric bleeding;

- in the postpartum period: increased level of postpartum septic diseases; neonatal hypoglycemia; hypogalactia; thyroid pathology.

Timely diagnosis and adequate glycemic control can significantly reduce complication rates and improve perinatal outcomes, as confirmed by randomized clinical trials [5, 6, 26, 29].

The main areas of improvement of pregnancy outcomes in women with GDM: full preconceptional preparation; strict maintenance of compensation ($HbA1c \leq 6.1\%$); control and normalization of blood pressure, monitoring of nephropathy, examination of the fundus, treatment of retinopathy; prevention of preeclampsia (acetylsalicylic acid, calcium); screening for asymptomatic bacteriuria and treatment; prolonging pregnancy to at least 36 weeks; taking folic acid 400 mcg/day for 6–12 months before pregnancy.

Women with gestational diabetes should give birth no later than 40+6 weeks of pregnancy using planned delivery (labor induction or cesarean section, if indicated). Elective delivery up to 40+6 weeks for women with gestational diabetes is used if there are complications on the part of the mother or fetus. Diabetes should not be considered a contraindication to attempting vaginal delivery after a previous cesarean section [7, 12, 17, 29].

Postpartum observation. After childbirth, glycemia normalizes in most women, but the risk of developing type 2 diabetes over the next 5–10 years remains high (up to 60 %). In this regard, it is recommended to perform a glucose tolerance test 6–12 weeks after delivery, followed by regular annual metabolic monitoring of glucose levels (fasting glucose or HbA1c).

Women with fasting glucose levels below 6.0 mmol/L ($HbA1c$ below 39 mmol/mol (5.7 %)) are unlikely to develop diabetes at this time and should continue to follow lifestyle advice after having a baby. They have a moderate risk of developing type 2 diabetes.

If the fasting plasma glucose level is between 6.0 and 6.9 mmol/L ($HbA1c$ between 39 and 47 mmol/mol (5.7 % and 6.4 %)), this indicates a high risk of developing type 2 diabetes. Such women are offered consultation with an endocrinologist and measures in accordance with protocols to prevent type 2 diabetes.

Women with a fasting glucose level of 7.0 mmol/L or higher ($HbA1c$ of 48 mmol/mol, 6.5 % or higher) are most likely to develop type 2 diabetes. These women should be offered a diagnostic test to confirm or rule out diabetes.

Important preventive measures include maintaining a normal body weight, following a balanced diet, engaging in physical activity, and informing the patient about modifying risk factors [2, 4, 15, 27, 28].

Conclusion

Gestational diabetes is a common complication of pregnancy with proven negative effects on maternal and perinatal outcomes.

Universal or selective screening with a glucose tolerance test enables timely detection of carbohydrate metabolism disorders.

Comprehensive management, including non-pharmacological measures and insulin therapy as indicated, reduces the risk of complications for both the mother and the fetus.

Postpartum follow-up is mandatory due to the high risk of developing type 2 diabetes.

Prospects for further research should be aimed at optimizing screening programs, assessing long-term metabolic consequences in children, and developing effective strategies for preventing diabetes in women after GDM.

References

1. American Diabetes Association Professional Practice Committee. 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024 Jan 1;47(Suppl 1):S282-S294. doi: 10.2337/dc24-S015.
2. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024 Jan 1;47(Suppl 1):S20-S42. doi: 10.2337/dc24-S002.
3. Bakiris E, Luiro K, Jokelainen J. Cardiovascular risk factors in women with previous GDM at age 46. *Acta Obstet Gynecol Scand*. 2024;103: n/a-n/a. doi: 10.1111/aogs.14861.
4. Bardugo A, Bendor CD, Rotem RS, Tsur AM, Derazne E, Gerstein HC, et al. Glucose intolerance in pregnancy and risk of early-onset type 2 diabetes: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2023 May;11(5):333-344. doi: 10.1016/S2213-8587(23)00062-1.
5. Cao Y, Sheng J, Zhang D, Chen L, Jiang Y, Cheng D, et al. The role of dietary fiber on preventing gestational diabetes mellitus in an at-risk group of high triglyceride-glucose index women: a randomized controlled trial. *Endocrine*. 2023 Dec;82(3):542-549. doi: 10.1007/s12020-023-03478-5.

6. Chatzakis C, Eleftheriades A, Demertzidou E, Dinas K, Vlahos N, Sotiriadis A, et al. Pregnancy outcomes in the different phenotypes of gestational diabetes mellitus based on the oral glucose tolerance test. A systematic review and meta-analysis. *Diabetes Res Clin Pract.* 2023;204:110913. doi: 10.1016/j.diabres.2023.110913.
7. Chen X, Du Y, Xia S, Li Z, Liu J. Vitamin B12 and gestational diabetes mellitus: a systematic review and meta-analysis. *Br J Nutr.* 2023 Apr 28;129(8):1324-1331. doi: 10.1017/S000711452200246X.
8. Crowther CA, Samuel D, McCowan LME, Edlin R, Tran T, McKinlay CJ; GEMS Trial Group. Lower versus Higher Glycemic Criteria for Diagnosis of Gestational Diabetes. *N Engl J Med.* 2022 Aug 18;387(7):587-598. doi: 10.1056/NEJMoa2204091.
9. Davis EM, Abebe KZ, Simhan HN, Catalano P, Costacou T, Comer D, et al. Perinatal Outcomes of Two Screening Strategies for Gestational Diabetes Mellitus: A Randomized Controlled Trial. *Obstet Gynecol.* 2021 Jul 1;138(1):6-15. doi: 10.1097/AOG.0000000000004431.
10. Desoye G, van Poppel M. Is a new discussion about diagnosis of gestational diabetes needed? *Lancet Diabetes Endocrinol.* 2024 Jan;12(1):11-12. doi: 10.1016/S2213-8587(23)00328-5.
11. Egan AM, Enninga EAL, Alrahmani L, Weaver AL, Sarra MP, Ruano R. Recurrent Gestational Diabetes Mellitus: A Narrative Review and Single-Center Experience. *J Clin Med.* 2021 Feb 3;10(4):569. doi: 10.3390/jcm10040569.
12. Goyette F, Wo BL, Iglesias MH, Rey E, Godbout A. Treatment of women with mild gestational diabetes mellitus decreases the risk of adverse perinatal outcomes. *Diabetes Metab.* 2023 Jul;49(4):101458. doi: 10.1016/j.diabet.2023.101458.
13. Gregory ECW, Ely DM. Trends and Characteristics in Prepregnancy Diabetes: United States, 2016-2021. *Natl Vital Stat Rep.* 2023 May;72(6):1-13. PMID: 37256333.
14. He Y, Ma RCW, McIntyre HD, Sacks DA, Lowe J, Catalano PM, et al. Comparing IADPSG and NICE Diagnostic Criteria for GDM in Predicting Adverse Pregnancy Outcomes. *Diabetes Care.* 2022 Sep 1;45(9):2046-2054. doi: 10.2337/dc22-0579.
15. Hirsch L, Shah BR, Berger H, Geary M, McDonald SD, Murray-Davis B, et al; for DOH-NET (Diabetes, Obesity and Hypertension in Pregnancy Research Network) and SOON (Southern Ontario Obstetrical Network) Investigators. Oral Glucose Tolerance Test Results in Pregnancy Can Be Used to Individualize the Risk of Future Maternal Type 2 Diabetes Mellitus in Women With Gestational Diabetes Mellitus. *Diabetes Care.* 2021 Aug;44(8):1860-1867. doi: 10.2337/dc21-0659.
16. Hill DJ, Hill TG. Maternal diet during pregnancy and adaptive changes in the maternal and fetal pancreas have implications for future metabolic health. *Front Endocrinol (Lausanne).* 2024 Sep 23;15:1456629. doi: 10.3389/fendo.2024.1456629.
17. Lambert V, Muñoz SE, Gil C, Román MD. Maternal dietary components in the development of gestational diabetes mellitus: a systematic review of observational studies to timely promotion of health. *Nutr J.* 2023 Mar 7;22(1):15. doi: 10.1186/s12937-023-00846-9.
18. Li N, Jiang J, Guo L. Effects of maternal folate and vitamin B12 on gestational diabetes mellitus: a dose-response meta-analysis of observational studies. *Eur J Clin Nutr.* 2022 Nov;76(11):1502-1512. doi: 10.1038/s41430-022-01076-8.
19. Li Y, Zhu Y, Zheng W, Gao Y, Huang R, Yang T, et al. The threshold effect of fasting blood glucose levels on the risk of delivering macrosomia in gestational diabetes mellitus patients. *Front Endocrinol (Lausanne).* 2025 May 29;16:1587306. doi: 10.3389/fendo.2025.1587306.
20. McIntyre HD, Kampmann U, Dalsgaard Clausen T, Laurie J, Ma RCW. Gestational Diabetes: An Update 60 Years After O'Sullivan and Mahan. *J Clin Endocrinol Metab.* 2024 Dec 18;110(1):e19-e31. doi: 10.1210/clinem/dgae709.
21. Mehrabadi A, Yu YH, Grandi SM, Platt RW, Filion KB. Gestational diabetes mellitus and subsequent cardiovascular disease in a period of rising diagnoses: Cohort study. *Acta Obstet Gynecol Scand.* 2025 Feb;104(2):331-341. doi: 10.1111/aogs.15022.
22. Mohan S, Egan AM. Diagnosis and Treatment of Hyperglycemia in Pregnancy: Type 2 Diabetes Mellitus and Gestational Diabetes. *Endocrinol Metab Clin North Am.* 2024 Sep;53(3):335-347. doi: 10.1016/j.ecl.2024.05.011.
23. Petry CJ. Nutrients as Risk Factors and Treatments for Gestational Diabetes. *Nutrients.* 2023 Nov 8;15(22):4716. doi: 10.3390/nu15224716.
24. Retnakaran R, Ye C, Hanley AJ, Connelly PW, Sermer M, Zinman B. Treatment of Gestational Diabetes Mellitus and Maternal Risk of Diabetes After Pregnancy. *Diabetes Care.* 2023 Mar 1;46(3):587-592. doi: 10.2337/dc22-1786.
25. Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. *Diabetes Res Clin Pract.* 2021 Feb;172:108642. doi: 10.1016/j.diabres.2020.108642.
26. Saravanan P, Sukumar N, Adaikalakoteswari A, Goljan I, Venkataraman H, Gopinath A, et al. Association of maternal vitamin B12 and folate levels in early pregnancy with gestational diabetes: a prospective UK cohort study (PRiDE study). *Diabetologia.* 2021 Oct;64(10):2170-2182. doi: 10.1007/s00125-021-05510-7.
27. Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, et al; TOBOGM Research Group. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. *N Engl J Med.* 2023 Jun 8;388(23):2132-2144.
28. Sobczyńska-Malefora A, Yajnik CS, Harrington DJ, Hitman GA, Finer S. Vitamin B12 and Folate Markers Are Associated with Insulin Resistance During the Third Trimester of Pregnancy in South Asian Women, Living in the United Kingdom, with Gestational Diabetes and Normal Glucose Tolerance. *J Nutr.* 2022 Jan 11;152(1):163-170. doi: 10.1093/jn/nxab352.
29. Sujan MAJ, Skarstad HMS, Rosvold G, Fougner SL, Nyrnes SA, Iversen AC, et al. Randomised controlled trial of preconception lifestyle intervention on maternal and offspring health in people with increased risk of gestational diabetes: study protocol for the BEFORE THE BEGINNING trial. *BMJ Open.* 2023 Oct 4;13(10):e073572. doi: 10.1136/bmjopen-2023-073572.
30. Wang H, Li N, Chiveste T, Werfalli M, Sun H, Yuen L, et al; IDF Diabetes Atlas Committee. Hyperglycaemia in Pregnancy Special Interest Group. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. *Diabetes Res Clin Pract.* 2022 Jan;183:109050. doi: 10.1016/j.diabres.2021.109050.
31. Xu R, Liu S, Zhong Z, Guo Y, Xia T, Chen Y, Ding L. The Influence of Maternal Folate Status on Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Nutrients.* 2023 Jun 16;15(12):2766. doi: 10.3390/nu15122766.
32. Yang Y, Cai Z, Zhang J. Association between maternal folate status and gestational diabetes mellitus. *Food Sci Nutr.* 2021 Feb 17;9(4):2042-2052. doi: 10.1002/fsn3.2173.

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