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КАФЕДРА АКУШЕРСТВА И ГИНЕКОЛОГИИ С КУРСОМ
ПОВЫШЕНИЯ КВАЛИФИКАЦИИ И ПЕРЕПОДГОТОВКИ

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ВЕДЕНИЕ БЕРЕМЕННОСТИ И РОДОВ У ЖЕНЩИН С САХАРНЫМ ДИАБЕТОМ

MANAGEMENT OF PREGNANCY AND CHILDBIRTH IN WOMEN WITH DIABETES

Учебно-методическое пособие

Минск БГМУ 2025

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Изложена основная информация по ведению беременности, родов и послеродового периода у женщин с сахарным диабетом.

Предназначено для студентов 4-го курса медицинского факультета иностранных учащихся.

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ABBREVIATIONS

BMI — body mass index
GMD — gestational diabetes mellitus
HbA1c — glycated hemoglobin
ICD-10 — International Classification of Diseases, 10th edition
OGTT — oral glucose tolerance test
T1D — diabetes type 1
T2D — diabetes type 1

MOTIVATIONAL CHARACTERISTIC OF THE SUBJECT

Theme of the seminar: «Management of pregnancy, labor and postpartum period in women with diabetes». The material is studied according to the thematic seminar plan for 4th year students of Medical Faculty of International Students.

PROBLEM REVIEW

Currently, worldwide prevalence of diabetes mellitus is rapidly increasing, leading to a so-called «hidden epidemic» in parallel with the epidemic of obesity: according to the statistics, diabetes mellitus has the highest prevalence rate among all endocrine disorders. Moreover, scientific prognosis is pessimistic: International Diabetes Federation (2021) states that 537 million of people aged 20–79 are currently suffering from the condition, and this figure is expected to increase to 643 million in 2030. Also, up to 21 million (16,7 %) of pregnancies are complicated by gestational diabetes mellitus (GDM).

In general, diabetes mellitus plays a crucial role in female reproductive health, negatively affecting menstrual cycle regulation and leading to its disruption, thus decreasing fertility, and leading to chronic anovulation. Diabetes in pregnancy increases the rates of spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, and neonatal respiratory distress syndrome, among others.

Timely diagnosis and correction of metabolic disturbances caused by diabetes mellitus, followed by prophylactic measures aimed at decreasing the risks of associated complications, is crucial not only during pregnancy, but also during preconception care.

Standards of care in pregnancy complicated by diabetes mellitus are specifically tailored according to specific physiological gestational changes in pancreatic function and peripheral insulin sensitivity.

Total duration of the lesson: 6 hours.

Aim of the lesson: provide detailed information concerning carbohydrates metabolic disturbances in pregnant women; study course of pregnancy and risks of potential complications; strategy of pregnancy, labor and postpartum management; prediction and prevention of gestational and perinatal complications in affected women and their offsprings.

Goals of the lesson:

1. Study physiological changes in carbohydrates metabolism during pregnancy.
2. Define indications for pregnancy termination in women with diabetes.
3. Learn up-to-date classification of diabetes mellitus, course of pregnancy, gestational and perinatal complications associated with diabetes mellitus.
4. Study methods of diagnostics and correction of carbohydrates metabolic disturbances in pregnancy.
5. Define strategy of pregnancy, delivery and postpartum period management aimed at prevention of complications.

Basic knowledge requirements:

For successful learning a student must revise earlier studied material in:

– human anatomy: pancreatic anatomy;

– normal physiology: pancreatic function and its regulation, insulin role in ovarian steroidogenesis;

– biological and bioorganic chemistry: structure and functions of pancreatic hormones;

– internal diseases: diagnostic methods used for evaluating condition and function of the pancreas.

Control questions on related disciplines:

1. Structure of the pancreas.
2. Pancreatic function and its regulation.
3. Chemical structure and biological action of pancreatic hormones.
4. Physical, laboratory and instrumental methods of diagnostics of pancreatic diseases.

Control questions on the topic of the class:

1. List the main physiological changes in carbohydrate metabolism during pregnancy, as well as changes in pancreatic function in pregnant women with previous pathology of carbohydrate metabolism.
2. Name the classification of diabetes mellitus according to ICD-10 and P. White.
3. Describe the course of pregnancy, possible gestational and perinatal complications, methods of correction of carbohydrate metabolism disorders in women with type 1 diabetes.

4. Describe the course of pregnancy, possible gestational and perinatal complications, methods of correction of carbohydrate metabolism disorders in women with type 2 diabetes mellitus.

5. Describe the course of pregnancy, possible gestational and perinatal complications, methods of correction of carbohydrate metabolism disorders in women with gestational diabetes mellitus.

6. List the indications for termination of pregnancy in pregnant women with diabetes mellitus.

STRUCTURE AND FUNCTION OF THE PANCREAS

Adult pancreas is 14–22 cm long, weighs 60–100 g, in shape the organ can be elongated, hammer-shaped, arc-shaped curved and angular. The pancreas has a head, corpus and tail, between the head and body there is a constriction — isthmus.

The gland has a lobular structure, each lobe is enclosed in an individual connective tissue framework. The stromal system of the gland includes its own capsule (adventitia), from which connective tissue trabeculae, dividing the gland into lobes, lobules and acini, pancreatic islets and shells, surrounded by vessels, nerves and ducts, extend deep into the organ.

The pancreas is a gland of both external and internal secretion. The exocrine function is to produce pancreatic juice, which plays an essential role in the digestive process. Four groups of pancreatic enzymes can be distinguished: proteases (chymotrypsin-gene, trypsinogen, aminopeptidase, etc.), lipases (esterase), carboanhydrases (maltase, amylase, lactase) and nucleases (deoxyribonuclease, ribonuclease).

The endocrine function of the pancreas is ensured by the activity of the islets of Langerhans, whose cells secrete insulin (beta cells), glucagon (alpha cells) and somatostatin (delta cells) into the blood.

Insulin is a hormone of protein nature, necessary for the regulation of carbohydrate metabolism, it provides glucose utilization in the organism: it increases the permeability of plasma membranes for glucose and other macronutrients, activates key enzymes of glycolysis, stimulates glycogen formation, increases protein and fat synthesis. Insulin has both anabolic and anti-catabolic effects.

Glucagon is a peptide hormone whose action is opposite to that of insulin: it activates gluconeogenesis, lipolysis and ketogenesis, and increases the catabolism of glycogen deposited in the liver. Thus, it is obvious that the physiological level of glucose in blood plasma is provided by the balance between insulin and glucagon secretion.

Somatostatin, synthesized by delta cells of the pancreas, inhibits the synthesis of insulin and glucagon.

CHANGES IN CARBOHYDRATE METABOLISM DURING PREGNANCY

Pregnancy is a special physiologic state in which certain changes in metabolic processes occur. Physiologically occurring pregnancy is characterized by two major changes in carbohydrate metabolism:

1. Ensuring continuous glucose supply to the embryo/foetus and chorion/placenta (transplacental glucose transport is mediated by glucose transporter proteins). Due to active glucose utilization and simultaneous activation of lipolysis and ketogenesis in the 1st trimester of pregnancy, it is particularly important to prevent hypoglycemic states and to ensure sufficient protein and fat intake.

2. Increase in insulin resistance from the 2nd trimester of pregnancy.

Peripheral tissue receptor sensitivity to insulin is a key component determining glucose homeostasis. Receptor sensitivity initially increases after embryo implantation, but decreases significantly after 12 weeks of gestation.

In the first weeks of pregnancy, the so-called feto-placental complex is formed — the concentration of growth hormone in the blood serum of the pregnant woman decreases, which leads to increased sensitivity of peripheral tissue receptors to insulin.

Later, with the onset of the 2nd trimester of pregnancy, the concentration in blood serum of such hormones as placental lactogen, progesterone, cortisol, prolactin and some others increases, which leads to a significant increase in insulin resistance of peripheral tissues, mainly adipocytes and skeletal muscles. Insulin resistance reaches its highest level by the end of the 3rd trimester and then significantly decreases in the postpartum period.

In addition to the above hormones, placental inflammatory mediators (e. g., tumor necrosis factor-alpha) and cytokines produced by adipose tissue influence tissue sensitivity to insulin. In particular, in the second half of pregnancy, leptin synthesis increases in adipocytes, while at the same time, due to prolactin exposure, leptin receptor resistance develops in the central nervous system, which reduces leptin transport across the blood-brain barrier, and leptin concentration in serum remains elevated. As a result of these processes, tissue sensitivity to insulin is reduced in order to maintain glucose homeostasis necessary for normal fetal development.

In normal pregnancy, the pancreas adapts to the increasing insulin resistance of peripheral tissues: under the influence of prolactin and placental lactogen, the number and volume of pancreatic beta-cells increase, and insulin synthesis increases. Due to the increased concentration and activity of glucokinase, the threshold level of glucose decreases, at which insulin synthesis is activated. An important role in maintaining glucose homeostasis is played by gluconeogenesis in the liver, the intensity of which increases in pregnant women.

CLASSIFICATION OF DIABETES MELLITUS IN PREGNANCY

Diabetes mellitus (DM) is a group of metabolic diseases characterized by chronic hyperglycaemia resulting from impaired insulin secretion, insulin action or a combination of these factors. Chronic hyperglycaemia in diabetes is associated with damage and dysfunction of various organs and systems (cardiovascular system, kidneys, visual organs, etc.).

At present, several variants of classification of DM in pregnant women are distinguished.

Coding according to ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th revision):

O24.3 Pre-existing diabetes mellitus unspecified

O24.4 Diabetes mellitus developed during pregnancy.

O24.9 Diabetes mellitus in pregnancy unspecified.

The code «O24.3 Pre-existing unspecified diabetes mellitus» includes two ICD-10 types: type 1 diabetes mellitus (E10) and type 2 diabetes mellitus (E11).

When diabetes is detected for the first time during pregnancy, overt diabetes should be differentiated from gestational diabetes.

Currently, the following classification is widely used in the Republic of Belarus, offered by P. White (Table 1).

Table 1

Modified classification of diabetes mellitus in pregnancy by P. White

Class	DM duration	Age of onset	Complications
A1 GDM, not requiring insulin	Any	Any	None
A2 GDM, requiring insulin	Any	Any	None
B	Less than 10	More than 20	None
C	10–19 Years	10–19 Years	None
D	More than 20	Less than 10	Non-proliferative retinopathy, arterial hypertension
F	C	Any	Nephropathy iii–iv stage (proteinuria over 0,5 g/24 h)
R	Any	Any	Proliferative retinopathy Ocular hemorrhage
F–R	Any	Any	Nephropathy, proliferative retinopathy
H	Any	Any	Ischemic heart disease
T	Any	Any	Transplanted kidney

In accordance with the annex to Resolution No. 88 of 10.12.2014 of the Ministry of Health of the Republic of Belarus, **medical reasons for terminating a pregnancy on the mother's part** include diabetes mellitus of classes F, R, F–R, T, and the state of clinical and metabolic decompensation from the first trimester of pregnancy.

ETIOLOGY AND PATHOGENESIS OF DIABETES MELLITUS

Type 1 Diabetes Mellitus

Type 1 diabetes mellitus (T1DM) is a polygenic multifactorial disease that leads to the development of absolute insulin deficiency and, as a consequence, to impaired carbohydrate and then other types of metabolism. In the majority of cases (70–90 %) in patients with T1DM there is evidence of an immune-mediated process — anti-bodies to pancreatic beta-cell antigens: autoantibodies to insulin (IAA), glutamate decarboxylase (GAD), tyrosine phosphatase-like protein (IA-2A), cytoplasmic islet cell antigens (ICA) and zinc transporters (ZnT8). The association of T1DM with the major histocompatibility complex (HLA) genes in the DQA, DQB loci has also been revealed.

The most frequent debut of T1DM occurs in childhood and adolescence, but the disease can develop at any age, up to senility. Manifestation is characterized by an acute onset, polyuria and thirst. Rapid deterioration of the condition and rapid progression of the pathologic process are noted: if T1DM occurs in childhood, by the end of the 1st year of the disease, residual insulin secretion by pancreatic beta-cells is practically absent. When the disease develops over 25 years of age, the manifestation of T1DM may be less pronounced, and deterioration of the condition is provoked mainly by acute or chronic stress and infectious diseases. According to current clinical guidelines and protocols, the diagnosis of T1DM implies the immediate administration of insulin therapy once the diagnosis has been confirmed.

Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is a disorder of carbohydrate metabolism, the pathogenetic cause of which is a combination of insulin resistance and secondary pancreatic beta-cell dysfunction. The specific aetiology of this disease has not been fully elucidated.

The primary cause is the development of insulin resistance in peripheral tissues, resulting in increased insulin synthesis at the beginning of the disease due to the need to ensure glucose homeostasis and compensate for insulin resistance. Prolonged course of T2DM depletes the compensatory capacity of pancreatic beta-cells, leading to their dysfunction.

The risk of developing T2DM increases with age, correlates with the severity of obesity and physical activity deficit. Gestational diabetes mellitus, arterial hypertension and dyslipidaemia have been found to be risk factors for the development of T2DM.

Diagnosis of T2DM is difficult due to the fact that hyperglycemia develops gradually, and clinical manifestations are less pronounced than in T1DM. Ketoacidosis is rare and is provoked mainly by infectious factors.

Insulin therapy is not mandatory for most people with T2DM, but may be required in severe disease and marked pancreatic beta-cell dysfunction.

Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is a disease characterized by hyperglycaemia that first occurs during pregnancy but does not meet the criteria for manifest DM (it is characterized by disturbance in blood glucose concentrations that existed before pregnancy but was only detected during pregnancy).

As described earlier, during pregnancy the sensitivity of peripheral tissues to insulin progressively decreases due to the influence of placental (lactogen, progesterone) and maternal (cortisol, oestrogens, prolactin) hormones. To maintain glucose homeostasis, insulin production increases and its clearance decreases, but in a number of pregnant women (especially with hereditary predisposition to the development of T2DM and obesity), the high demand for insulin exceeds the functional reserve of pancreatic beta-cells, which leads to hyperglycemia. Thus, from the pathogenetic point of view, GDM represents T2DM and is a multifactorial disease, the development of which is influenced by both genetic predisposition and epigenetic factors.

Risk factors for developing GDM include:

1. Pregestational:

– excessive body weight (BMI more than 25 kg/m^2) or obesity (BMI more than 30 kg/m^2);
– weight gain of more than 10 kg after the age of 18 years;
– age of the pregnant woman over 40 years old;
– mongoloid race;
– family history of DM;
– history of GDM;
– polycystic ovary syndrome;
– smoking.

2. Gestational:

– pregnancy resulting from in vitro fertilization;
– multifetal gestation;
– use of beta-adrenoblockers or glucocorticosteroids during pregnancy;
– pathologic weight gain during pregnancy;

– irrational diet with a predominance of easily digestible carbohydrates;
– low level of physical activity.

In most cases, GDM does not have a vivid clinical picture, which is characteristic of the debut of GDM.

The symptoms of hyperglycaemia may be characteristic of the onset of DM, and the symptoms of hyperglycaemia may be considered typical of pregnancy (e. g., increased urination or fatigue). This necessitates routine screening of pregnant women for GDM.

COMPLICATIONS OF PREGNANCY WITH DIABETES MELLITUS

Diabetes mellitus during pregnancy significantly increases the risk of complications, which include:

– hypertensive disorders (pre-eclampsia, eclampsia, gestational hypertension);
– large fetus and clinical mismatch between fetal and pelvic size;
– birth trauma (both maternal and fetal);
– the need for surgical delivery (cesarean section, assisted vaginal delivery — obstetric forceps, vacuum-assisted delivery);
– multifetal gestation;
– bleeding in the 3rd period of labor and early postpartum;
– infectious complications in the postpartum period;
– risks for the newborn: macrosomia, hypertrophic cardiomyopathy, respiratory distress syndrome, hypoglycemia, hyperbilirubimia, hypocalcemia, polycythemia.

Therefore, as mentioned above, DM in pregnancy significantly increases the risk of both maternal and perinatal morbidity and mortality.

Children born to mothers with diabetes, regardless of type, have a significantly increased risk of metabolic and neurological disorders such as T1DM, metabolic syndrome, and delayed cognitive development.

GDM significantly increases the risk of developing a number of **remote complications** for women, including:

– impaired glucose tolerance, which occurs in 30 % of postpartum women;
– T2DM, with a 9.5 — fold increase in the risk of developing T2DM after GDM, with the highest probability within the first 5 years after childbirth;
– metabolic syndrome (abdominal obesity, arterial hypertension, insulin resistance, increased atherogenicity index), which is experienced by up to 30 % of women giving birth within 5 years after delivery;
– cardiovascular diseases (the risk of myocardial infarction and/or stroke increases twofold after GDM).

DIAGNOSIS OF DIABETES MELLITUS DURING PREGNANCY

Diagnosis should be made to detect abnormalities of carbohydrates metabolism in all pregnant women in order to initiate timely therapy and prevent maternal and perinatal complications.

Complaints and anamnesis

In most cases of diabetes mellitus during pregnancy, there is no specific clinical picture. The main symptoms (frequent urination, weakness, fatigue, decreased concentration and memory) may be considered by the patient as manifestations of pregnancy.

When collecting the history, it is necessary to:

– actively identify complaints that may be associated with DM: polyuria, polydipsia, polydipsia, polyuria, polydipsia, thirst;

– clarify family history of T1DM and T2DM;

– clarify the presence of GDM in previous pregnancies;

– clarify the birth weight of children in previous pregnancies, the presence of fetal malformations, multiple fetuses;

– carefully collect a gynecologic history: ask about menstrual irregularities and symptoms.

– identify menstrual problems and symptoms characteristic of polycystic ovary syndrome;

– assess the presence of risk factors, which may include: arterial hypertension, dyslipidemia, taking medications (beta-adrenoblockers, glucocorticosteroids), hypodynamia, irrational diet.

Physical examination

There are no specific signs of diabetes mellitus manifesting during pregnancy that can be detected by physical examination.

A standard general clinical examination of the pregnant woman should be performed, with emphasis on pre-pregnancy BMI calculations and weight dynamics during pregnancy.

Laboratory diagnostics

Laboratory diagnosis is currently the «gold standard» for detecting diabetes mellitus in pregnant women.

In the Republic of Belarus, according to the clinical protocol «Medical supervision and provision of medical care to women in obstetrics and gynaecology»

dated 2018, when monitoring the course of a normal pregnancy it is necessary to perform

– fasting glycaemia study at the first antenatal clinic visit (before the 12th week of pregnancy);

– fasting blood glucose test at 24 weeks' gestation;

– oral glucose tolerance test (OGTT) at 24–28 weeks' gestation;

– consultation with an endocrinologist at the first antenatal clinic visit, then — to assess the results of the OGTT and if indicated.

Glucose should only be measured in venous plasma, not in serum or whole capillary blood. The use of individual blood glucose meters has no diagnostic value in confirming the diagnosis of diabetes mellitus and can only be recommended for self-monitoring of blood glucose when the diagnosis is established.

When diabetes mellitus is first diagnosed during pregnancy, a distinction must be made between overt diabetes mellitus and gestational diabetes mellitus.

Overt diabetes mellitus is «true», i. e. non-gestational, diabetes mellitus that is first identified during pregnancy. Overt DM can be either type 1 or type 2.

Diagnostic criteria for overt (first diagnosed) diabetes mellitus during pregnancy are given in Table 2.

Table 2

Diagnostic criteria for overt (first diagnosed) diabetes mellitus during pregnancy

Parameters	Criteria
Fasting serum glucose	≥ 7,0 mmol/L
Glycated hemoglobin (HbA1c)	≥ 6,5 %
Serum glucose regardless of time and meals if accompanied by symptoms of hyperglycaemia, or 2 hours after glucose consumption during OGTT	≥ 11,1 mmol/L

Glycated hemoglobin (HbA1c) is a specific compound of hemoglobin in erythrocytes with glucose, the concentration of which reflects the average blood glucose level over the lifespan of the erythrocyte (on average, for three months).

According to the recommendations of the World Health Organization, normal level of HbA1c is considered to be up to 6.0 %, while HbA1c level exceeding 6.5 % indicates diabetes. HbA1c level in the range of 6.0 to 6.5 % can't be used as an isolated criterion for a diagnosis of diabetes, but it does not rule out the possibility of diagnosing diabetes based on the level of glucose in fasting venous blood.

Gestational diabetes can be diagnosed by a single determination of plasma glucose concentration on any day of pregnancy when fasting venous plasma glucose level is in the range of ≥ 5.1 mmol/L but < 7.0 mmol/L.

Oral glucose tolerance test (OGTT) with 75g of glucose is recommended for all pregnant women without pregestational diabetes, who have not shown any

carbohydrate metabolism disorders in the first half of pregnancy or have not been screened earlier, between 24–28 weeks of gestation.

The optimal time for conducting OGTT is between 24–28 weeks of pregnancy. However, this test can be performed up to 32 weeks of gestation in cases of high risk of GDM, large fetal size according to ultrasound examination, presence of ultrasound signs of diabetic fetopathy, and disproportionate fetal size.

OGTT is considered a safe diagnostic test, but there are **contraindications**, such as:

– gestational or manifest diabetes mellitus diagnosed before 24 weeks of pregnancy,

– strict bed rest in hospital due to obstetric indications (such as clinically significant cervical insufficiency with high risks of premature delivery),

– clinical and laboratory signs of acute inflammatory diseases,

– gastrointestinal diseases in the acute stage of exacerbation,

– severe nausea and/or vomiting.

Steps and rules of performing OGTT. The test should be conducted while on a normal diet (at least 150 g of carbohydrates per day) for three days prior to the examination. The test should be performed in the morning, after an eight-hour overnight fast, with the last meal in the evening containing no less than 30–50 g of carbohydrates. Drinking water before the test is allowed. During the test, the patient should remain seated. Medications that can affect glucose levels (multivitamins, iron supplements, glucocorticoids, beta-blockers, beta-agonists) should be taken after completing the test, if possible.

Steps:

The first stage involves collecting the first sample of plasma from fasting venous blood.

The second stage requires drinking a solution consisting of 75 g of dry glucose dissolved in 250–300ml of warm drinking water within 5 minutes.

The third stage involves determining the level of glucose in venous plasma 1 and 2 hours after glucose loading.

Diagnostic criteria for gestational diabetes during OGTT are presented in Table 3.

Table 3

Diagnostic criteria for gestational diabetes during OGTT

Time	Glucose concentration in serum, mmol/l
Fasting	≥ 5,1 – <7,0
After 1 hour	≥ 10,0
After 2 hours	≥ 8,5 – <11,1

Important: A diagnosis of gestational diabetes mellitus can be made if venous plasma glucose ≥ 5.1 mmol/L is detected at any gestational age, including after an OGTT that does not reveal abnormalities in carbohydrate metabolism.

MANAGEMENT OF DIABETES MELLITUS DURING PREGNANCY

Management of pregnancy complicated by DM should be done in conjunction with an obstetrician-gynaecologist, endocrinologist, general practitioner, ophthalmologist, and nephrologist.

Non-pharmacological treatment

First of all, in order to prevent obstetric and perinatal complications, lifestyle modification is recommended, i. e. changes in diet and physical activity.

Dietary therapy involves the restriction of carbohydrates with a high glycaemic index and trans fats, while to meet the needs of the mother and foetus, the daily amount of carbohydrates should be at least 40 % of the calculated daily glycaemia and ketone bodies in the urine. Foods containing carbohydrates are distributed throughout the day into 3 main and 2–3 additional meals. Each meal should include slowly digestible carbohydrates, proteins, mono- and polyunsaturated fats, dietary fibre (at least 28 g/day in total).

Calorie restriction is required for pregnant women with pre-pregnancy obesity (BMI more than 30 kg/m^2) and with abnormal weight gain during pregnancy, but the caloric intake should not be less than 1800 kcal/day, otherwise the risk of ketonuria increases.

Regular aerobic aerobic exercise of at least 150 minutes per week is recommended in the absence of obstetric contraindications: walking (including Nordic walking), swimming, training on an exercise bike. Modified yoga and Pilates classes are also recommended, with the exclusion of exercises that impede venous return to the heart.

Injury-prone physical activities are contraindicated: mountain and water skiing, snowboarding, equestrian sports, contact and gambling sports, jumping, scuba diving.

Glucose levels management

All pregnant women with diabetes are recommended to perform daily self-monitoring of blood glucose levels until the end of pregnancy. Self-monitoring should be carried out by the patient using portable devices (glucometers) that have undergone mandatory calibration.

Glycaemic self-monitoring targets should be followed as follows:

– fasting glucose should be less than 5.1 mmol/l;

– glucose 1 hour after the main meals (breakfast, lunch, dinner) should be less than 7.0 mmol/l;

– glucose 2 hours after the main meals (breakfast, lunch, dinner) should be less than 6.7 mmol/l.

If the patient is only on nutritional therapy, self-monitoring of glycaemia is required daily in the morning on an empty stomach and 1 hour after the start of the main meals.

If a patient is prescribed insulin therapy in addition to diet therapy, self-monitoring of blood glucose may be performed **more frequently (according to the endocrinologist's prescriptions)**:

– in the morning after fasting;

– before main meals to calculate the dose of bolus insulin for the meal and correct hyperglycemia;

– 1 hour after the start of main meals;

– in the evening before bedtime;

– at 3 am and additionally at any time when needed.

All pregnant women with diabetes are recommended to keep a self-monitoring diary. This should record blood glucose levels, the time and amount of food consumed, and the time and type of physical activity.

Insulin therapy

Insulin therapy regimen and type of insulin preparations are selected individually.

In GDM, insulin therapy is recommended if it is impossible to achieve target glycaemic values (two or more off-target glycaemic values while following dietary and physical activity recommendations) during 1–2 weeks of self-monitoring.

If manifest DM is detected, it is recommended to perform basal bolus insulin therapy: basal insulin should be administered once at bedtime, bolus insulin should be divided into 3 injections 15–20 minutes before the main meals in proportions: 40 % before breakfast, 30 % before lunch and dinner. Dose titration is carried out under glycaemic control every 3 days until target glycaemic levels are achieved.

The use of oral hypoglycaemic agents is not routinely recommended for GDM. If a woman has been taking these medications (e. g. metformin) before pregnancy, they should be discontinued at the onset of pregnancy, but taking metformin early in pregnancy is not an indication for termination of pregnancy.

Conditions requiring urgent medical assistance: hypoglycemic and hyperglycemic coma

Hypoglycaemic coma is the most common complication of T1DM and is less common in T2DM and GDM.

Hypoglycaemic states are most often caused by over-dosing of insulin preparations, increased physical activity with an unchanged diet and insulin therapy, eating disorders (late meals or insufficient carbohydrate intake), and changes in insulin therapy.

Coma most often occurs at glycaemia less than 2.8 mmol/l, but in some cases of prolonged hyperglycaemia, clinical manifestations of hypoglycaemic states may occur at higher glucose concentrations.

The clinic of hypoglycaemic states changes progressively with the severity of cerebral hypoxia and includes:

– adrenergic symptoms: tachycardia, tremors, restlessness, pale skin, increased sweating, nausea, intense hunger, aggressive behaviour;

– neuroglucopenic symptoms: weakness, decreased concentration, dizziness and headache, paresthesias, fear, disorientation,

Clinical manifestations of hypoglycaemic states progressively change in response to the severity of cerebral hypoxia.

Hypoglycaemic state is characterised by a rapid onset of symptoms: from the onset of the first symptoms to the onset of coma may take only a few minutes.

Hypoglycaemic states are distinguished from hyperglycaemic states by: moist skin, muscle hypertonicity with possible twitching, hyperreflexia, dilated pupils, absence of acetone odour.

If consciousness is maintained, treatment consists of ingestion of easily digestible carbohydrates in liquid form (tea, fruit juice) or in the form of a glucose tablet. After the hypoglycaemia has subsided, a meal containing «slow» carbohydrates is indicated.

If hypoglycaemic coma develops, it is necessary to ensure that the oral cavity is free, remove dentures if present. Emergency treatment includes intravenous infusion of 20–60 ml of 40 % glucose solution, but the rate of infusion should not exceed 10 ml/min, as faster infusion may cause hypokalaemia.

The main cause of hyperglycaemic coma is diabetic ketoacidosis (DKA), which is based on absolute or significant relative insulin deficiency.

Diabetic ketoacidosis is an acute decompensation of diabetes requiring emergency hospitalisation, accompanied by hyperglycaemia (glucose level > 13 mmol/l), hyperketonaemia (> 5 mmol/l), ketonuria, metabolic acidosis (pH < 7.3) and impaired consciousness.

Causes of DKA include undiagnosed T1DM, inadequate insulin therapy, and dietary errors. Pregnancy is a separate risk factor for the development of DKA due to the characteristic changes in carbohydrate metabolism described above.

Clinical manifestations of DKA include: severe thirst and polyuria, loss of appetite, nausea, acetonuria, muscle weakness, dry skin, tachycardia. In decompensation of DKA and the development of precoma, there is an odour of acetone in the exhaled air, lethargy, apathy, oliguria, abdominal pain, and rigid forced breathing.

In hyperglycaemic coma, there is loss of consciousness, noisy, interrupted breathing, arterial hypotension, oliguria, tachycardia, hypothermia.

The following causes can be fatal: decreased potassium levels, cardiac arrest, hypovolaemic shock, thrombosis, acute kidney injury. The principles of DKA treatment are based on rehydration, insulin administration, correction of electrolyte balance, restoration of the acid-base state, and restoration of the acid-base state.

PREGNANCY MONITORING IN WOMEN WITH DIABETES MELLITUS

Pregnancy monitoring in women with DM is carried out in accordance with the clinical protocol «Medical monitoring and medical care for women in obstetrics and gynaecology» of 2018 (Table 4).

Table 4

Pregnancy monitoring in women with DM

Management	T1DM	T2DM	GDM
Antenatal clinic visits	From the onset of pregnancy up to 12 weeks — once every 30 days; after 12 weeks — once every 14 days; after 30 weeks — weekly		
Fetal ultrasound	Routine screening intervals: 11–13 6/7 weeks, 18–21 weeks, 32–35 weeks of gestation additional: 36 weeks of gestational with Doppler		
In addition to routine antenatal monitoring	Keeping a self-monitoring diary, checking glycated haemoglobin levels once per trimester, undergoing urinalysis after 30 weeks, once every 7 days, consulting and following up with a general practitioner, consulting with an ophthalmologist for eye fundus examination once a trimester, and consulting with a urologist when indicated		
	Urinalysis for ketone bodies at every visit to the gynecological clinic; urinalysis for daily protein loss as indicated; urinalysis using the Nechiporenko method upon registration and once per trimester; urine culture and sensitivity testing once per trimester; nasal, throat, and vaginal swab culture once per trimester; biochemical blood analysis as indicated.		None

End of the table 4

Management	T1DM	T2DM	GDM
Non-pharmacological treatment	A diet excluding easily digestible carbohydrates should be followed; a daily self-monitoring diary, including the number of bread units (BU), insulin doses, blood glucose levels, and physical activity		
Insulin therapy	Required	Is administered when target glycemic levels are not achieved without insulin therapy for two weeks	
	Intensified insulin therapy should be administered in a basal-bolus regimen using genetically engineered human insulin or insulin analogues in doses that depend on the level of glycemia, physical activity, and carbohydrate intake, taking into account changes in insulin requirements throughout pregnancy, under the supervision of an endocrinologist		
Planned hospitalizations to either endocrinological or therapeutic departments of the hospital.	Before 12 weeks of gestation, at 20–22 weeks and 28–32 weeks for follow-up, examination and insulin therapy regimen optimization	If insulin therapy is necessary. An endocrinologist consultation should be scheduled at 30-32 weeks of pregnancy. Hospitalization if required	Before 12 weeks of gestation, at 20–22 weeks, 28–32 weeks, 36–38 weeks in case of insulin therapy
Hospitalization before delivery in the pathology department of a maternity hospital	36–38 weeks of gestation	38 weeks of gestation	

SPECIFICS OF FETAL ULTRASOUND IN PREGNANT WOMEN WITH DIABETES MELLITUS

Fetal ultrasound examination in women with diabetes should include:

– standard fetometry, percentile estimation of fetometric parameters and fetal weight;

– identification of phenotypic and visceral signs of diabetic fetopathy.

– determination of fetal maturity (Beklar's nucleus — the largest size of the secondary ossification point of the distal femoral epiphysis);

– assessment of placenta thickness, amniotic fluid quantity, umbilical cord condition;

– doppler assessment of utero-fetal-placental blood-circulation.

Antenatal diagnosis of diabetic fetopathy is performed basing on:

– asymmetric macrosomia: increase in abdominal circumference more than 90 percentile for gestational age at normal head size and femur length;

– phenotypic signs: double contour of the head due to soft tissue oedema, thickness of subcutaneous fatty tissue of the neck more than 0.32 cm, thickness of subcutaneous fatty tissue of the chest and abdomen more than 0.5 cm;

– visceral signs: hepatomegaly, cardiomegaly (increased cardiothoracic index more than 25 %).

LABOR AND POSTPARTUM

Terms and methods of delivery

The choice of the term and method of delivery in pregnant women with DM should be based on the assessment of the fetal condition and the presence of obstetric complications. It is recommended to determine the delivery tactics no later than 36-38 weeks of gestation.

For T1DM and T2DM with severe complications of pregnancy (pre-eclampsia, chronic placental insufficiency, renal dysfunction, etc.), the optimal time of delivery is 37–38 weeks of gestation, as prolongation of pregnancy to 39 weeks or more increases the risk of fetal macrosomia, clinical mismatch of fetal and pelvic size, leading to a higher likelihood of birth trauma and the need for surgical delivery.

Preterm delivery (before 37 full weeks of pregnancy) is necessary in case of deteriorating foetal condition, worsening gestational complications (pre-eclampsia), increasing severity of diabetes complications (retinopathy, nephropathy).

Any type of DM is not in itself an indication for caesarean section.

In pregnant women with DM the indications for surgical delivery are:

– estimated fetal weight of more than 4000 g;

– diabetic fetopathy according to ultrasound findings;

– breech presentation of the foetus;

– signs of intrauterine fetal distress;

– severe and/or progressive complications of DM (haemorrhages on the ocular fundus and other ocular abnormalities, increasing proteinuria and/or acetonuria, etc.).

The preferred method of delivery in DM is by programmed delivery through natural labour. Regular fetal monitoring (cardiotocography) is required during the whole period of labor.

To prevent birth-related injuries, the fetal head should be delivered between contractions, after performing an episiotomy.

For spontaneous and abdominal deliveries, the preferred method of anaesthesia is prolonged epidural anaesthesia.

Glucose levels management in labor and postpartum

During labour and the postpartum period, it is important to monitor blood glucose levels. If a vaginal delivery or planned caesarean section is scheduled, the pregnant woman should not eat in the morning and should be given a dose of short-acting insulin based on her blood glucose level. Long-acting insulin (basal insulin) should not be administered or should be given at half the usual dose.

As the labor progresses, blood glucose control should be monitored every 4–6 hours (using a portable glucometer or in a laboratory) with the administration of short-acting insulin as necessary.

Intravenous infusion of 5% glucose solution is permissible to maintain glucose levels within the range of 3.9–6.9 mmol/L. When blood glucose levels reach 7.0 mmol/L or higher, short-acting insulin should be administered intravenously at a dose of 2–4 units per hour (as a bolus or using an infusion pump) until target glucose levels are achieved.

Immediately after giving birth, the need for insulin sharply decreases or is absent altogether. At the same time, the maximum low level of glycemia is characteristic for the first three days of the postpartum period, which must be taken into account when correcting the insulin therapy regimen. By the 7th–10th day of the postpartum period, the need for insulin is restored to the level that existed in the woman before pregnancy.

Postpartum period specifics

There are almost no contraindications for breastfeeding in cases of type 1 and 2 diabetes. The exception may be women with severe complications, such as progressing diabetic nephropathy, which requires the use of medications that are transferred into breast milk.

To suppress lactation, dopamine agonists are used according to the generally accepted scheme:

– cabergoline 1 mg orally once during the first day after delivery;

– bromocriptine 2.5 mg orally per day during childbirth, followed by 2.5 mg twice a day for 14 days.

In cases of type 2 diabetes during breastfeeding, insulin therapy should be continued if target glycemic levels cannot be achieved through diet alone. The use of oral hypoglycemic agents during lactation may cause hypoglycemia in the infant.

After lactation cessation, patients require consultation with an endocrinologist to select oral hypoglycemic and symptomatic therapy, as well as to continue monitoring and correcting diabetic complications. Women with gestational diabetes should be recommended to undergo an oral glucose tolerance test 4–12 weeks after

delivery if the fasting venous plasma glucose level is less than 7.0 mmol/L. After delivery, carbohydrate metabolism can normalize in most women with GDM.

If hyperglycemia persists and/or insulin is required, it may indicate manifest diabetes, and an endocrinologist should be consulted. It is important to note that 25–50 % of women who have had GDM may develop true diabetes over time. Women with a history of GDM are at high risk of recurrence of this complication during subsequent pregnancies.

TASKS FOR SELF-ASSESSMENT

Clinical case

Pregnant N., 25 years old, came to the antenatal clinic at 24 weeks of pregnancy for a routine examination. Objectively: height — 167 cm, body weight — 93 kg, weight gain during pregnancy — 15 kg. From the anamnesis: menstrual cycle is irregular, before the pregnancy was diagnosed as «polycystic ovary syndrome», the pregnancy occurred as a result of in vitro fertilization due to anovulatory infertility and lack of effect of medical treatment. According to examination results: fasting venous plasma glycaemia — 6.2 mmol/l, traces of glucose in the general urine analysis.

Questions:

1. Primary diagnosis?
2. Is it necessary to perform an oral glucose tolerance test to clarify the diagnosis?
3. What is the strategy of correction of carbohydrate metabolism disorders in this case?

Answers:

1. 24 weeks' pregnancy. Gestational diabetes mellitus.
2. OGTT is not required, as the results of fasting glycaemia are a sufficient basis for the diagnosis.
3. A diet with the exclusion of easily digestible carbohydrates is prescribed; keeping a diary of self-monitoring daily (obligatory) with indication of the number of bread units, insulin doses, glycaemia, physical activity. Insulin therapy is prescribed in the absence of achieving target glycaemic levels without insulin therapy for 2 weeks; in the basal-bolus regime with genetically engineered human insulin or insulin analogues in doses depending on the level of glycaemia, physical activity, the number of meals, taking into account changes in insulin requirements throughout pregnancy (under the supervision of an endocrinologist).

TEST CONTROL

1. A physiological pregnancy is accompanied by:

a) absence of changes in carbohydrate metabolism;
b) an increase in insulin resistance;
c) increased sensitivity of peripheral receptors to insulin;
d) decrease in insulin synthesis.

2. Insulin therapy is an obligatory method of treatment of:

a) Type 1 diabetes mellitus;
b) type 2 diabetes mellitus;
c) gestational diabetes mellitus;
d) all types of diabetes mellitus.

3. The adverse effects of gestational diabetes mellitus on the foetus are due to:

a) hyperglycaemia;
b) hypoglycaemia;
c) hyperinsulinaemia;
d) hypoinsulinaemia.

4. Oral glucose-tolerance test is performed at gestational age:

a) 10–12 weeks;
b) 16–17 weeks;
c) 24–28 weeks;
d) after 37 weeks.

5. The diagnosis of «manifest diabetes mellitus» can be made when:

a) fasting venous plasma glucose level < 5.1 mmol/l;
b) fasting venous plasma glucose level between 5.1–7.0 mmol/l;
c) fasting venous plasma glucose level ≥ 7.0 mmol/l;
d) fasting venous plasma glucose level ≥ 11.1 mmol/l.

6. The diagnosis of «gestational diabetes mellitus» may be made:

a) when fasting venous plasma glucose level < 5.1 mmol/l;
b) when the fasting venous plasma glucose level is between 5.1–7.0 mmol/l;
c) when fasting venous plasma glucose level ≥ 7.0 mmol/l;
d) only after an oral glucose tolerance test.

7. Gestational diabetes mellitus can be treated with all but:

a) non-medical methods of treatment (diet correction, dosed physical activity);
b) oral sugar-lowering drugs;
c) genetically engineered human insulin preparations.

8. Indications for surgical delivery in pregnant women with diabetes mellitus are all except for:

a) suspected large fetal size (weight more than 4000 g);
b) breech presentation of the foetus;
c) the need for insulin therapy;
d) evidence of intrauterine fetal distress.

9. Pregestational risk factors for the development of gestational diabetes mellitus include all but:

a) overweight and/or obesity;
b) being over 40 years of age;
c) presence of polycystic ovary syndrome;
d) body weight deficiency.

10. Breastfeeding is contraindicated in the following conditions:

a) any type of diabetes mellitus;
b) diabetes mellitus requiring insulin therapy;
c) gestational diabetes mellitus;
d) diabetes mellitus complicated by severe diabetic nephropathy.

Answers: 1 — b, **2** — a, **3** — a, **4** — c, **5** — c, **6** — b, **7** — b, **8** — c, **9** — d, **10** — d.

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