SECTION 3. MEDICINE

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3.1 Modern concepts of preeclampsia pathogenesis and screening approaches in pregnancy

According to the World Health Organization (WHO), severe preeclampsia and eclampsia remain among the most common and severe complications of pregnancy, childbirth, and the postpartum period. According to the literature, the global incidence of preeclampsia (PE) varies from 4.6% to 9.7%, and that of eclampsia from 0.1% to 1.9% [48]. According to leading scientists and clinicians, this situation is primarily associated with the poor health status of women of reproductive age, the influence of harmful anthropogenic factors, adverse socioeconomic conditions, and negative cultural impacts.

Meta-analytical studies indicate that in 44.7–52.1% of pregnant women suffering from hypertensive disorders, the course of pregnancy is complicated [49, 50, 51]. Thus, in 15.6–20.9% of this category of patients, the first trimester proceeds with mild vomiting; in 0.8–2.7%, with excessive vomiting; in 10.2–15.5%, there is a threatened miscarriage; in 7.1–15.9%, premature labor occurs; placental dysfunction is observed in 28.1–32.7% of cases; and signs of fetal growth restriction are diagnosed in 24.3–52.8% of clinical cases. During labor, there is a significantly higher frequency of premature rupture of membranes (28.8–43.7%), labor anomalies (32.3–40.8%), fetal distress (27.2–30.5%), and early postpartum hemorrhages (11.3–19.8%). In 19.7–25.2% of cases, the course of PE does not respond to medication, which is also a significant factor in the increased rates of operative delivery and maternal trauma.

It should be emphasized that, in the structure of obstetric causes of maternal mortality, massive obstetric hemorrhages and thromboembolic complications have occupied the leading position worldwide for several decades. Severe preeclampsia/eclampsia and postpartum purulent-septic complications, particularly obstetric sepsis, alternately occupy the second and third places.

An important prerequisite for reducing the frequency and severity of hypertensive disorders during pregnancy, or the risks of their occurrence, is the development of new and improvement of existing screening methods for the diagnosis of subclinical disorders and their broad implementation in practical obstetrics at the stage of antenatal clinics or by family physicians. It is known that the high sensitivity and specificity of screening programs directly depend on their etiopathogenetic orientation. PE is a multifactorial pathological condition; its mechanism is quite complex and multivectoral, which determines the necessity of continuing clinical research in meta-analytical formats, exchanging experience, and conducting active discussions aimed at improving the effectiveness of prenatal preparation of women, management tactics, treatment, and rehabilitation.

According to the literature, many concepts explaining the occurrence of preeclampsia currently exist. However, they can be united under several leading directions and pathogenetic frameworks into a single modern model consisting of several stages (Figure 1).

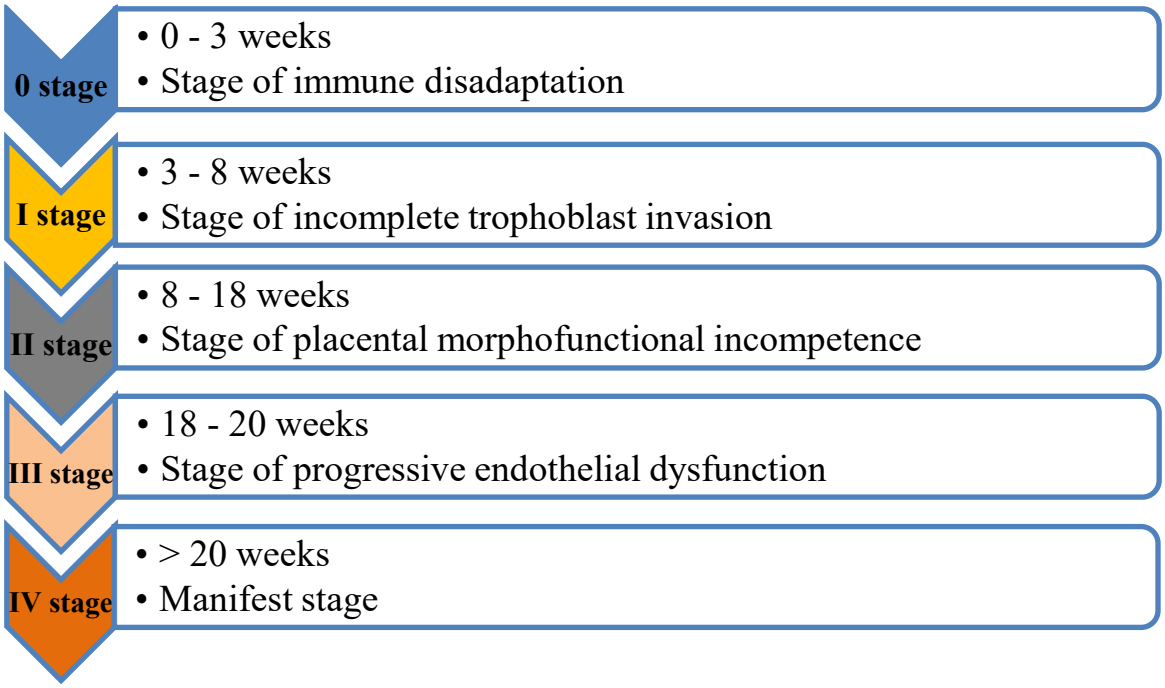

Figure 1. Stages of preeclampsia development [made by the authors]

So, most researchers consider as the triggering factor, and therefore the first stage in the development of PE, the inhibition of proliferative and migratory activity

of trophoblast cells with aberrant remodeling of uterine spiral arteries as pregnancy progresses [52]. It is known that these terminal branches of the uterine arteries supply blood to the intervillous spaces of the placenta and, in physiological pregnancy, undergo gestational remodeling of their muscular layer, providing a progressive increase in uteroplacental blood flow according to the gestational age. In PE, under the influence of genetic, immunological, and histochemical factors, disturbances in the processes of placentation and insufficient transformation of the muscular layer of the uterine spiral arteries occur. This leads to hemodynamic disturbances, vasospasm of the uteroplacental complex vessels, and a decrease in intervillous blood flow because of persistent sensitivity to vasoactive stimuli [53]. Consequently, this results in chronic hypoxia of the uteroplacental complex tissues and gradual impairment of their functional and biochemical activity.

It should be emphasized that some researchers distinguish a so-called “zero stage” of PE development, which at present remains a controversial issue due to the lack of consistent studies and systematic analysis of the available data. Nevertheless, according to statements concerning the “zero stage” of PE development, two factors may serve as significant preconception etiopathogenetic links: 1) the absence of genetically determined integrity in the spermatozoon fertilizing the oocyte, that is, the presence of so-called extensive sperm DNA fragmentation, and 2) HLA homozygosity of a married couple. According to the limited available studies, pathological fragmentation of sperm DNA may result from three main molecular mechanisms — congenital abnormalities of chromatin structure, destabilizing effects of reactive oxygen species associated with depletion of the antioxidant system, and abortive apoptosis. An increase in HLA homozygosity, reduction in antigenic diversity between spouses, and polymorphism of HLA-C and HLA-G sublocus antigens are also believed by researchers to contribute to the development of preeclampsia as pregnancy progresses [54]. At present, it has been established that maternal immune tolerance toward the fetus and regulation of the immune response are fundamental factors ensuring pregnancy progression and its physiological, uncomplicated course. Expression of HLA-proteins (HLA-C, HLA-E, HLA-F, and HLA-G) in

cytotrophoblast cells ensures suppression of natural killer (NK) cell cytotoxic activity by interacting with killer cell immunoglobulin-like receptors (KIR receptors), thereby preventing NK-mediated cytotoxicity. These mechanisms also exert a significant regulatory influence on the processes of gestational remodeling of the vascular component of the uteroplacental complex. Therefore, in our opinion, the "zero stage" of PE development demonstrates causal relationships and thus should be taken into account and incorporated into the modern concept of pathogenesis.

According to research, the "second stage" of PE formation develops between the 8th and 18th weeks of gestation and is characterized by the absence of clinical signs of PE. During this gestational period, under physiological conditions, the process of cotyledon formation - the main structural and functional units of the mature placenta - should be fully completed, and the appropriate gestational transformations in the branches of the spiral arteries of the endometrium and, critically, the myometrium should occur. The biological rationale for these changes lies in the need to ensure the autonomy of uteroplacental blood flow through the transformation of spiral arteries into vascular channels with low resistance to blood flow and insensitivity to vasoactive stimuli in the organism.

An important link in the pathogenesis of PE is limited and insufficient remodeling of spiral arteries, which leads to the preservation of muscular and elastic elements along the entire vessel length, or more commonly, in the myometrial segment. This preserves their sensitivity to vasoactive stimuli, enhances hypoxic and reoxygenation reactions, damages the intervillous space, and results in the formation of a stable pathological capillary blood flow in the placenta, as well as chronic oxidative stress.

According to modern views, during the subsequent "third stage" of PE development, disturbances in the morphofunctional competence of the placenta cause the pathological release of trophoblastic factors such as vascular endothelial growth factor (VEGF), placental growth factor (PlGF), pregnancy-associated plasma protein-A (PAPP-A), placental protein 13 (PP-13), soluble fms-like tyrosine kinase-1 (sFlt-1), and soluble endoglin (sEng) [55]. An analysis of literature sources shows that most

researchers agree that the imbalance of placental factors plays a leading role in the development of the maternal inflammatory response observed in PE, which in turn leads to the clinical manifestation of this pregnancy complication.

In their studies, authors have demonstrated a moderate-to-strong correlation between significantly low serum concentrations of VEGF, PlGF, PAPP-A, and PP-13 in pregnant women during the first trimester (10–13 weeks) and the severity of PE. This provides an analytical basis for predicting and early diagnosis of PE, as well as for timely pharmacological correction according to modern clinical protocols.

Endogenous antiangiogenic proteins sFlt-1 and sEng, which are able to neutralize the proangiogenic properties of VEGF and PIGF and exacerbate endothelial dysfunction, are also of great importance in the pathogenesis of PE. An increase in the concentration of sFlt-1 and sEng with a simultaneous decrease in the level of free fractions of VEGF and PIGF precedes the development of PE and is a prognostic factor for its severe course.

Recently, the effect of microRNAs, in particular miR-126 and miR-210, on the processes of vasculogenesis and angiogenesis in the placenta in pregnant women with PE, as well as placental metabolism under hypoxia, has been actively studied [56, 57]. MicroRNAs are short non-coding RNAs located in the cytoplasm of endothelial cells and play an important role in the translation and degradation of mRNA, regulating gene expression.

It has been found that miR-126 (vascular endothelial growth factor D) plays a key role in the development and functioning of blood vessels of the fetoplacental complex, regulation of vascular homeostasis, and has antithrombotic and anti-inflammatory properties. According to the results of the study, patients with PE showed decreased expression of miR-126, which caused impaired expression of the antiangiogenic gene PIK3R2 (regulates cell proliferation and function) and had a negative effect on PI3K-Akt signaling pathways. Decreased expression of miR- 126 was also accompanied by a positive correlation with the level of VEGF microRNA.

Studies on the role of **miR-210** in the development of PE have shown that during the **first trimester** of physiological pregnancy, an intensification of **miR-210**

expression occurs, which is necessary to enhance metabolic and proliferative reactions, particularly during the early stages of placental morphofunctional structure formation. In severe PE, prolonged and excessive **miR-210 expression** occurs, affecting trophoblast migration and invasion. In several scientific works, a targeted analysis of specific **miR-210 genes** was conducted, namely **potassium channel modulatory factor 1 (KCMF1)**, **coenzyme Q**, and **hydroxysteroid (17-β) dehydrogenase 1 (HSD17B1)**. The results showed that in pregnant women with PE, **miR-210 levels** increased before the appearance of major clinical symptoms and led to reduced invasion of villous trophoblasts through a mechanism dependent on **mitogen-activated protein kinase (MAPK)**.

Thus, progressive endothelial dysfunction and tissue hypoxia of the uteroplacental complex initiate a cascade of multidirectional metabolic disorders characteristic of PE, defining the final, **fourth stage** of its formation - the "manifest stage." It is known that the leading pathognomonic clinical sign of PE is **arterial hypertension**.

According to modern research, several mechanisms of **vasospasm** in PE are distinguished. In particular, the accumulation of free radicals and peroxidation compounds leads to excessive tension and depletion of the antioxidant system, activation of **cyclooxygenase** and **lipoxygenase** pathways of **linoleic, linolenic,** and **arachidonic acid** metabolism, resulting in significant alterations in the phospholipid composition of cellular biomembranes. Disturbance of the lipid layer of membranes limits the functionality of **Ca^{2+} and Mg^{2+} ion channels** and induces contraction of vascular smooth muscle [58].

The second mechanism of systemic vasospasm in PE is caused by the effect of oxidative stress on the synthesis of **thromboxane (TxA_2)**, **prostacyclin (PGI_2)**, and **prostaglandins PGE, $PGF_2\alpha$**. An increase in **TxA_2** levels with a simultaneous decrease in **PGI_2** synthesis leads to generalized vasoconstriction and changes in the rheological properties of maternal blood [59].

Another possible mechanism of hypertension in PE, according to modern studies, is the **activation of neutrophils**, which, under conditions of imbalance

between oxidant aggression and antioxidant protection, excessively produce **elastase**, **protease**, and **oxygen free radicals**. This leads to increased vascular permeability with the formation of **persistent antiphospholipid syndrome** and a **chronic form of disseminated intravascular coagulation (DIC)** [60]. Under these conditions, endothelial cells produce **endothelins**, which have a vasoconstrictor effect. Endothelial damage is accompanied by increased platelet aggregation and adhesion, leading to the formation of **cell-fibrin microconglomerates** that obstruct microcirculation.

The fourth mechanism of systemic vasoconstriction in PE is associated with decreased activity of **nitric oxide (NO)** — an **endothelium-dependent relaxing factor**, which under physiological pregnancy reduces platelet aggregation and facilitates cardiovascular adaptation to gestational hypervolemic hemodilution. It has been proven that the effect of nitric oxide directly depends on the level of **prostacyclin**, and therefore its activity is reduced in pregnant women with PE [61].

The last, **fifth possible mechanism** of arterial hypertension in PE, according to scientists and clinicians, is explained by the formation of **specific fetal antigens**, which naturally appear after the **20th week of gestation** in the fetal organism. Under physiological conditions, the maternal organism counteracts this through the synthesis of antibodies via the **HLA histocompatibility system**. However, in cases of impaired placentation and endothelial dysfunction, active fetal antigens enter the maternal systemic circulation in large quantities and participate in complex immunological reactions, forming **circulating immune complexes (CICs)** [62]. Studies have shown that CICs, which may contain components of the complement system such as **C1q, C3, and C4**, can deposit on the walls of cerebral and parenchymal organ vessels (kidneys, liver, lungs), leading to **endotheliosis** and **morphological damage**. It has been found that in severe PE, there is an increase in the concentration of **soluble vascular cell adhesion molecule-1 (sVCAM-1)** — an inflammatory protein that stimulates the release of proinflammatory cytokines and can serve as a marker of endotheliosis and a prognostic factor for PE development [63].

In addition, as a result of immune-inflammatory reactions caused by the influence of CICs, the following pathological changes occur:

1. **Decreased deformability of erythrocytes** with increased rigidity and stiffness of their membranes, leading to reduced oxygen capacity of the blood and impaired O_2 and CO_2 exchange;

2. **Activation of platelet adhesive and aggregative properties** with an imbalance in the prostanoid system of pressor and relaxing action, along with excessive serotonin formation, which enhances arterial hypertension, peripheral vascular resistance, and contributes to the development of **thrombohemorrhagic syndrome** with microcirculatory disorders, tissue hypoxia, and cellular damage;

3. **Dysfunction of the kallikrein-kinin system**, which plays a leading role in blood coagulation and fibrinolysis, in immune and inflammatory responses, affects the **renin-angiotensin system**, and is associated with the **complement system** [64].

According to modern concepts of PE pathogenesis, the direct consequences of the **microcirculatory crisis** are an increase in blood levels of under-oxidized metabolic products, elevated osmotic pressure, chronic hypovolemia, and **multiple organ dysfunction** (primarily hepatic and renal failure), the severity of which determines the course and intensity of this pregnancy complication.

Thus, increasing disturbances of cellular and tissue metabolism are accompanied by the accumulation in tissues and biological fluids of **endogenous toxic substances**, namely end metabolites and intermediate metabolic products in high concentrations, products of **active proteolysis of plasma proteins**, **peroxidation products**, **proteolytic and lipolytic enzymes**, and others, which initiate the formation of the **endogenous intoxication syndrome**. In this case, endotoxicosis may be caused not only by the increase of certain substances but also by the **disturbance of balance between antagonistic compounds**.

In turn, the increased excretion of **degradation products of proteins, lipids, phospholipids, peroxidation compounds, and other toxic metabolites**, against the background of pathological changes in the renal parenchyma, inevitably leads to disturbances in the **homeostatic, filtration, and nitrogen-excreting functions of the kidneys** [65].

Under conditions of profound microcirculatory disorders, chronic tissue

hypoxia, and pathological hypercoagulation, hepatic failure gradually develops [66]. The progression of PE leads to a decrease in the activity of microsomal enzymes, particularly cytochrome P-450, which catalyze oxidation reactions of organic substances, ensuring the metabolism of endogenous compounds (steroids, fatty acids) and xenobiotics. A decrease in hepatic enzymatic function in pregnant women with PE results in the accumulation of toxic metabolites in the organism, such as unconjugated bilirubin, glutamine, steroids, bile acids, free fatty acids, ammonium, mercaptans, and products of intestinal digestion (phenol, indole, skatole), which possess endotoxin properties and exacerbate the pathological state of the organism. Hepatorenal failure affects the condition of the morphofunctional structures of the gastrointestinal mucosa and the intestinal microbiocenosis, which exerts a pronounced detoxifying effect on both exogenous and endogenous toxins.

Thus, the pathogenetic mechanisms of PE development depend on multiple factors and are complex and multifactorial. However, their further study and analysis are of utmost importance for improving algorithms of management of patients with PE and for appropriate screening and monitoring of pregnant women in risk groups, with the goal of optimizing approaches to early diagnosis and prevention of PE.

Diagnostic Criteria for Preeclampsia

Preeclampsia *de novo*:

• Gestational hypertension arising at or after 20 weeks of gestation;

• Accompanied by ≥ 1 of the following new conditions: proteinuria or other maternal organ dysfunctions (Table 1).

Table 1. Maternal organ dysfunction in preeclampsia

Maternal organ dysfunction	Complications
AKI	Creatinine ≥ 90 μmol/L
Liver damage	Elevated transaminases (ALT or AST > 40 IU/L) with or without pain in the right upper quadrant or epigastric region
Neurological lesions	Eclampsia, altered mental status, blindness, stroke, clonus, severe headache, and persistent visual scotomata
Hematologic disorders	Thrombocytopenia (PLT < 150,000/μL), disseminated intravascular coagulation, hemolysis
Uteroplacental dysfunction	Fetal growth restriction, abnormal umbilical artery Doppler findings, or stillbirth

Superimposed preeclampsia on chronic hypertension

In women with chronic essential hypertension, an increase in blood pressure alone is insufficient for diagnosing superimposed preeclampsia. Superimposed preeclampsia is characterized by:

• The development of any of the above-mentioned maternal organ dysfunctions;

• New-onset proteinuria against a background of increased blood pressure;

• Proteinuria associated with kidney disease during pregnancy is not sufficient for the diagnosis of superimposed preeclampsia.

Depending on the timing, perinatal, and maternal complications, the condition is classified as Early-onset preeclampsia (EOP) — delivery before 34 weeks of gestation; Late-onset preeclampsia (LOP) — delivery at or after 34 weeks of gestation or later.

According to FIGO recommendations, preeclampsia may be further subdivided

into non–mutually exclusive subclasses:

1. Early-onset preeclampsia (with delivery at < 34^{+0} weeks of gestation).

2. Preterm preeclampsia (with delivery at < 37^{+0} weeks of gestation).

3. Late-onset preeclampsia (with delivery at ≥ 34^{+0} weeks of gestation).

4. Term preeclampsia (with delivery at ≥ 37^{+0} weeks of gestation) [67].

Using a Bayesian model, it is possible to effectively predict and prevent early-onset and preterm preeclampsia; the rates of early-onset and preterm PE may be reduced by 80% and 60%, respectively.

The "screening and prevention" strategy for PE in the first trimester of pregnancy has been approved by FIGO and harmonized with the FMF.

First-trimester screening for preeclampsia

Comprehensive first-trimester screening for PE includes maternal factors and a series of biological parameters measured at 11–13^{+6} weeks of gestation:

1. Maternal characteristics, medical and obstetric history;

2. Mean arterial pressure (MAP);

3. Biochemical marker of PlGF. In resource-limited countries, if PlGF is unavailable, PAPP-A is used instead;

4. Uterine artery pulsatility index (UtA-PI) [68].

The aim of early screening is to identify the high-risk group, since earlier initiation of prophylactic measures is particularly effective in preventing EOP, which causes the most severe pregnancy complications and necessitates delivery before 34 weeks of gestation [69].

Maternal characteristics, history, and obstetric conditions

According to the recommendations of the Ministry of Health of Ukraine and international professional bodies (USPSTF, FIGO, ACOG, NICE), the high-risk factors for PE development include:

- Hypertensive disease during a previous pregnancy;
- Chronic kidney disease;
- Autoimmune disorders such as systemic lupus erythematosus or antiphospholipid syndrome;

- Type 1 or type 2 diabetes mellitus;
- Chronic hypertension.

Moderate-risk factors include:

- First pregnancy;
- Maternal age ≥ 40 years;
- Interpregnancy interval > 10 years;
- Body mass index (BMI) ≥ 35 kg/m² at the first prenatal visit;
- Family history of preeclampsia;
- Multiple pregnancy.

If one high-risk factor or two moderate-risk factors are present, the pregnant woman is classified as at risk of PE development [68, 70–72].

The Fetal Medicine Foundation (FMF) provides a free online calculator for risk assessment based on maternal history. Parameters included are:

• Maternal characteristics (date of birth, height, weight, ethnicity, smoking);

• Current pregnancy (last menstrual period, "vanishing twin," conception method);

• Gestational age determination (conception method, gestational term, estimated delivery date);

• Medical history (chronic hypertension, type I or II diabetes, maternal history of PE, systemic lupus erythematosus, antiphospholipid syndrome);

• Obstetric history (no previous pregnancies ≥ 24 weeks, or at least one pregnancy ≥ 24 weeks). (see: https://fetalmedicine.org/research/assess/preeclampsia)

It is not possible to reliably predict PE risk using only maternal factors. However, combining maternal and fetal parameters significantly improves the prediction of early-onset PE in high-risk women.

Mean Arterial Pressure

Blood pressure is measured after five minutes of rest on both arms twice, at one-minute intervals. The MAP is calculated based on systolic and diastolic blood pressure values, which are automatically recalculated by the risk calculator according to the formula: **MAP = DBP + (SBP – DBP)/3.**

Placental Growth Factor and Pregnancy-Associated Plasma Protein

PlGF is a proangiogenic protein produced by the trophoblast that participates in placental angiogenesis; it is the most studied and the best biochemical marker of PE. The level of PlGF increases according to gestational age up to 26–30 weeks in a normal pregnancy. A decrease in PlGF occurs due to developing placental insufficiency. In preeclampsia, which is closely pathogenetically related to placental dysfunction, the PlGF level is significantly lower or even abnormally low in the first trimester compared with normal pregnancies. Thus, PlGF is a specific marker for detecting the development of preeclampsia at early gestational stages, which is especially important for diagnosing early-onset preeclampsia.

PAPP-A is an embryo-specific protein produced by the placenta and decidual membrane. The maternal serum level of PAPP-A continuously increases with gestational age, showing the greatest rise at the end of pregnancy. Low PAPP-A levels in maternal serum at 9–13 weeks of gestation are associated with possible fetal chromosomal abnormalities (trisomies 21, 13, or 18) and subsequent development of PE, fetal growth restriction, and spontaneous preterm labor. The diagnostic sensitivity of reduced PAPP-A levels alone for PE remains low, but when combined with Doppler indices of uterine artery PI, sensitivity increases significantly.

Uterine Artery Pulsatility Index

The use of the **pulsatility index (PI)** to assess uterine artery resistance in the context of PE screening is recommended by the **International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)** [73] and is part of the comprehensive PE screening recommended by the **FMF**. **UtA-PI** is defined as the ratio of the difference between maximum and minimum blood flow velocities to the mean blood flow velocity in the vessel. UtA-PI decreases with increasing gestational age, with maternal age, and weight in the first trimester, but increases again in the third trimester. In women who experienced PE in a previous pregnancy, UtA-PI is inversely related to gestational age at delivery, being high in those who deliver preterm. Using combined screening models including uterine artery Doppler, the detection accuracy of early PE can reach up to 90%.

According to **FIGO** recommendations, screening is conducted in two stages when resources are limited. At the **first stage**, in women during the first trimester, maternal risk factors and MAP are routinely assessed; if PE risk is detected, the **second stage** includes determination of PlGF or PAPP-A and UtA-PI.

An online calculator for individualized PE risk assessment is freely available on the FMF website: https://courses.fetalmedicine.com/calculator/pe?locale=en

Prevention of Preeclampsia

Pregnant women identified as high risk for PE after first-trimester screening should receive **aspirin** from **11–14^{+6} to 36 weeks of gestation** at a dose of ~150 mg daily in the evening. In women with low calcium intake, calcium supplementation is recommended as part of antenatal care to prevent PE in all pregnant women, especially in high-risk cases (up to 1 g of elemental calcium daily). Therapy initiated after 20 weeks of gestation is considered ineffective.

Monitoring in Asymptomatic Women

For asymptomatic pregnant women at high risk of PE, assessment should include:

• increasing awareness of symptoms and home blood pressure monitoring;

• regular formal clinical examinations including measurement of blood pressure, assessment of proteinuria, hemoglobin, platelet count, serum creatinine, and liver transaminases;

• ultrasound evaluation of fetal growth and Doppler assessment of umbilical and uterine arteries.

Maternal Monitoring in Preeclampsia

In pregnant women with PE, maternal assessment should include: blood pressure monitoring, repeated proteinuria testing, clinical assessment, and blood tests for hemoglobin, platelet count, liver, and renal function twice weekly. Regardless of the hypertensive disorder, blood pressure consistently at or above **140/90 mmHg** requires urgent treatment**.** For **mild hypertension**, first-line medications are **oral methyldopa, labetalol**, or **nifedipine**. For **severe hypertension**, first-line agents include **oral nifedipine or labetalol**, or **intravenous labetalol or hydralazine**. The target **DBP** is

85 mmHg; if DBP drops below 80 mmHg, antihypertensive therapy should be reduced or discontinued.

Proteinuria is determined qualitatively (≥ 2+ using a urine dipstick) and quantitatively (≥ 0.3 g/24h in a full 24-hour urine collection) or as **protein/creatinine ratio (PrCr) ≥ 30 mg/mmol**, or **albumin/creatinine ratio (ACR) ≥ 8 mg/mmol**. For the diagnosis of PE, proteinuria is not mandatory, especially in women with renal disease, except in cases of newly developed hypertension.

To prevent seizures, women with **severe hypertension and proteinuria** should receive **magnesium sulfate** before and for at least 24 hours after delivery.

Fetal Monitoring in Preeclampsia

Upon first diagnosis of PE, **ultrasound biometry** should be performed to assess fetal weight (including biparietal diameter, head and abdominal circumference, and femur length), amniotic fluid volume, and Doppler studies of the umbilical and uterine arteries. When fetal growth restriction is confirmed, serial assessment of fetal growth, amniotic fluid volume, and umbilical artery Doppler should be performed every two weeks from **24 weeks of gestation until delivery**. Between **24^{+0} and 34^{+0} weeks** (up to **38^{+0} weeks** in cases of planned cesarean section), **antenatal corticosteroids** should be administered for fetal lung maturation. Before **32 weeks of gestation**, **magnesium sulfate** should be given for fetal neuroprotection.

Prediction of Maternal and Fetal Complications in Preeclampsia

After comprehensive screening, women with suspected PE and those with chronic hypertension should undergo testing that includes components of the **fullPIERS** and **PREP-S** models at least twice weekly to identify women at increased risk of adverse maternal outcomes.

Adverse maternal and neonatal outcomes are cumulative indicators based on the **Duffy consensus study** (Table 2) [74].

Table 2. Major adverse outcomes in preeclampsia

Maternal outcomes	Neonatal outcomes
• Maternal death • Eclampsia • Stroke • Cortical blindness • Retinal detachment • Pulmonary edema • Acute kidney injury • Hepatic hematoma or liver capsule rupture • Placental abruption • Postpartum hemorrhage • Elevated liver enzymes • Low platelet count • Requirement for admission to the intensive care unit • Intubation and mechanical ventilation (not related to delivery)	• Stillbirth • Gestational age at birth • Birth weight • Small for gestational age • Neonatal death • Neonatal seizures • Requirement for admission to the neonatal unit • Respiratory support

Integrated risk assessment models (fullPIERS and PREP-S) help identify women at high risk of complications, allowing timely interventions to minimize risks and improve maternal and fetal outcomes. The **FullPIERS model** can be used at any gestational age; the **PREP-S model** applies only up to 34 weeks.

fullPIERS is a free online tool designed to assess the likelihood of adverse outcomes in women with PE within 48 hours or 7 days from baseline. Factors considered in the model include gestational age, presence or absence of chest pain or dyspnea, oxygen saturation, platelet count, creatinine, and AST/ALT (see

https://preempt.bcchr.ca/evidence/fullpiers). A diagnosis of PE, if angiogenic imbalance is present, will be confirmed [75, 76].

Management decisions regarding inpatient or outpatient care for PE are based on risk thresholds — for example, hospitalization is recommended at a **risk ≥ 10%**, and **≥ 30%** indicates the highest risk of adverse outcomes.

PREP-S is a free online calculator for assessing the likelihood of PE-related adverse outcomes from 2 to 42 days after diagnosis, applicable in pregnancies up to **34^{+6} weeks**. Model factors include maternal age, gestational age at diagnosis, presence/absence of tendon reflexes, comorbidities (hypertension, renal disease, diabetes, autoimmune disorders, prior PE), systolic BP (mmHg), oxygen saturation, platelet count ($\times 10^9$/L), urea (mmol/L), creatinine (μmol/L), protein/creatinine ratio (mg/mmol), and whether the woman received any antihypertensive or magnesium sulfate therapy at or within 24 hours of diagnosis (https://www.evidencio.com/models/show/1038).

According to calculations, women with a **predicted complication probability below 50%** may avoid unnecessary referral to tertiary centers and remain under outpatient observation. Women with high or very high risk should be hospitalized for continuous intensive monitoring.

Conclusion

Preeclampsia leads to severe obstetric complications and affects the subsequent development of target organ diseases (kidneys, liver, brain, and cardiovascular system). Currently, there is no guaranteed method to prevent preeclampsia; however, early and consistent monitoring of pregnant women and management of potential risk factors can help reduce the likelihood of complications. Therefore, early detection of pathogenic abnormalities and timely preventive and therapeutic interventions remain a **priority task of the modern medical community**.