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SMJERNICE
GUIDELINES

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Hrvatsko društvo za perinatalnu medicinu

PROCJENA RIZIKA ZA PREEKLAMPSIJU

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Smjernice

Preeklampsija je čest uzrok maternalnog i perinatalnog morbiditeta i mortaliteta, posebice kada se pojavi rano. Premda razumijevanje patogeneze preeklampsije nije u potpunosti jasno, sadašnja teorija objašnjava njezin nastanak u dvije faze. **Prva faza** je uzrokovana slabom invazijom trofoblasta, što rezultira neadekvatnim preoblikovanjem spiralnih arterija. Pretpostavlja se da ovo vodi do **druge faze**, koja uključuje **majčin odgovor na endotelnu disfunkciju i neravnotežu između angiogenih i antiangiogenih čimbenika**, što se manifestira kliničkim simptomima bolesti. Predviđanje nastanka preeklampsije u prvom tromjesečju trudnoće potaknuto je željom da se identificiraju trudnice s visokim rizikom za preeklampsiju, što će omogućiti da se s potrebnim mjerama započne dovoljno rano kako bi se poboljšala placentacija, spriječila bolest ili barem smanjila njezina učestalost. Preeklampsija je gestacijski poremećaj odnosno sindrom koji definiraju **sistolički krvni tlak ≥140 mmHg i / ili dijastolički krvni tlak ≥90 mmHg, izmjeren najmanje dva puta u vremenskom razmaku od 4 sata u prethodno normotenzivne trudnice, uz prisutnost proteinurije od ≥0,3g/L u 24-satnom uzorku urina.**

Tablica 1. Simptomi teške preeklampsije

• Krvni tlak ≥ 160 i/ ili 110 mmHg, ukoliko se izmjeri dva puta unutar 4 sata dok trudnica leži
• Proteinurija ≥ 0,3g/L /24-satnom urinu
• Oligurija (500 mL ili manje u 24 sata)
• Glavobolja ili smetnje s vidom
• Bol u epigastriju
• Edem pluća ili cijanoza
• Trombocitopenija
• Kreatinin > 90 µmol/L
• Transaminaze > 40 IU/L
• DIK
• IUGR
• Rani početak preeklampsije prije 34. tjedna trudnoće udružen je s visokim rizikom kratkoročnog i dugoročnog maternalnog i perinatalnog morbiditeta.
• Kasni početak preeklampsije je nakon 34. tjedna trudnoće.

Smjernice za procjenu rizika za prvo tromjesečje trudnoće

Procjena rizika za razvoj preeklampsije (između 11.–14. tjedna trudnoće) se sugerira uraditi u slučaju identifikacije 1 velikog rizičnog čimbenika* ili 2 umjerena čimbenika rizika**

Tablica 2. Skupina trudnica s visokim rizikom za razvoj preeklampsije*

• Hipertenzivna bolest tijekom prethodne trudnoće i pridružene komplikacije (HELLP sindrom, abrupcija placente, IUGR, mrtvorođenost)
• Kronična hipertenzija
• Kronična bolest bubrega
• Autoimune bolesti poput sistemskog eritemskog lupusa
• Stečena trombofilija (antifosfolipidni sindrom)#
• Nasljedna trombofilija (mutacija gena za protrombin ili faktor V, deficit AT, proteina C i proteina S)
• Dijabetes tipa 1 i tipa 2

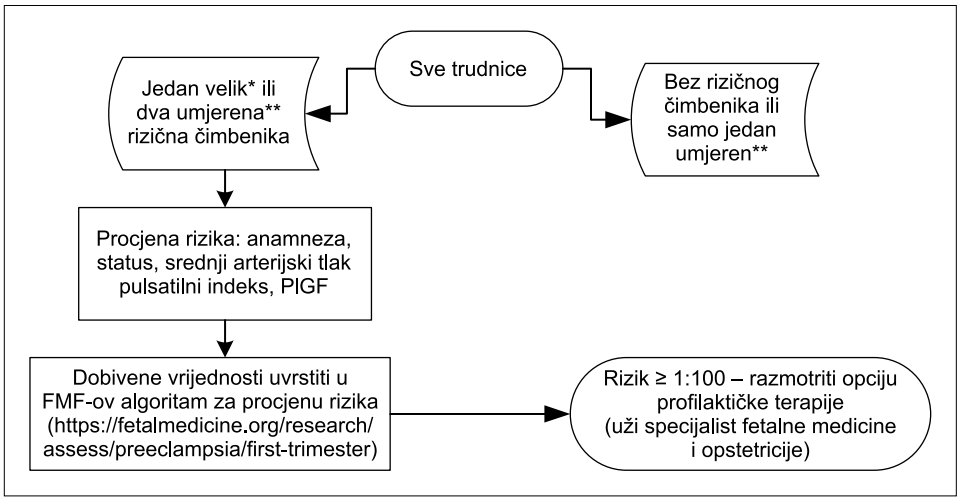
#U slučaju dijagnoze antifosfolipidnog sindroma, sugerira se terapija aspirinom i heparinom

Tablica 3. Skupina trudnica s umjerenim rizikom za razvoj preeklampsije**

• Prva trudnoća
• Dob trudnice > 40 godina
• Vremenski razmak između dvije trudnoće > 10 godina
• Indeks tjelesne mase > 35 kg/m2
• Gestacijski dijabetes
• Obiteljska anamneza preeklampsije
• Blizanačka trudnoća
• Trudnoća nakon izvantjelesne oplodnje

* Skupina trudnica s visokim rizikom za razvoj preeklampsije

** Skupina trudnica s umjerenim rizikom za razvoj preeklampsije



Shema 1. Smjernice za procjenu rizika za prvo tromjesečje trudnoće

Procjena rizika uključuje:

- Obiteljsku, osobnu i opstetričku anamnezu trudnice
- Status trudnice (životna dob, tjelesna visina, tjelesna masa, indeks tjelesne mase, krvni tlak, srednji arterijski tlak)
- Pulsatilni indeks uterine arterije)
- Biomarker PlGF

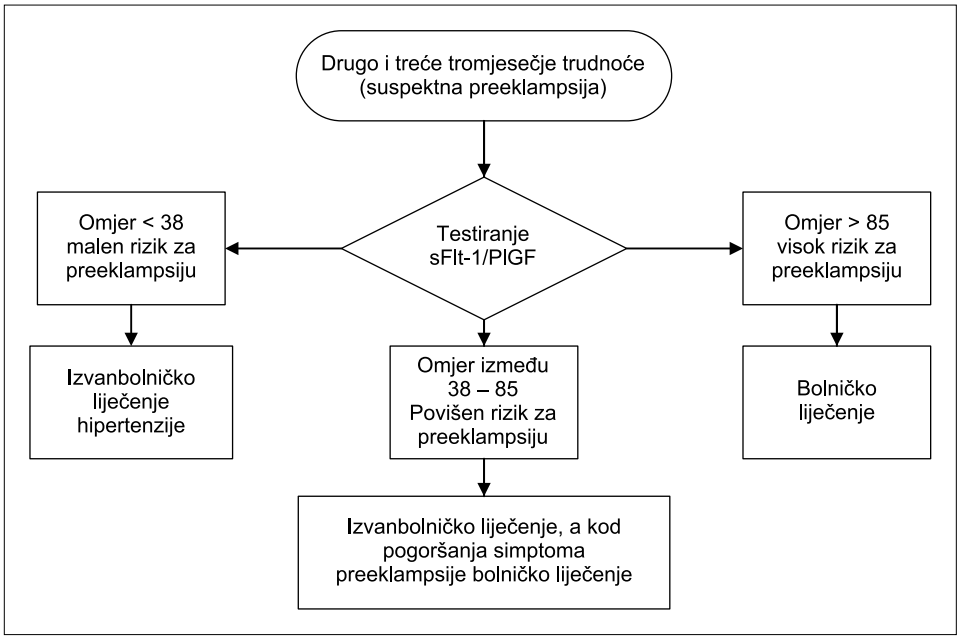
Potom se vrijednosti uvrštavaju u FMF-ov algoritam za procjenu rizika razvoja preeklampsije (ili neki drugi, akreditirani algoritam za procjenu rizika preeklampsije) (https//fetalmedicine.org//research/assess/preeclampsia) te uslučaju rizika većeg od 1:100 razmotriti uvođenje profilaktične terapije aspirinom***

Smjernice za procjenu rizika za drugo i treće tromjesečje trudnoće

Nakon 20. tjedna trudnoće preporuča se korištenje **omjera sFlt-1/PlGF** u svrhu procjene rizika za razvoj preeklampsije, koji, uz kliničku procjenu, može pomoći u predviđanju ili isključivanju nastanka preeklampsije.

Za predviđanje rane preeklampsije (20. do 34. tjedan) unutar 4 tjedna, granične vrijednosti za Elecsys sFlt-1/PlGF su između 38 i 85, a vrijednosti > 85 impliciraju rani razvoj preeklampsije.

Za predviđanje kasne preeklampsije (nakon 34. tjedna) unutar 4 tjedna, granične vrijednosti za Elecsys sFlt-1/PlGF su između 38 i 110, a vrijednosti > 110 impliciraju kasni razvoj preeklampsije.



Shema 2. Smjernice za procjenu rizika za drugo i treće tromjesečje

*** Profilaktičku terapiju indicira uži specijalist iz fetalne medicine i opstetricije

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RISK ASSESSMENT FOR PREECLAMPSIA

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Guidelines

Preeclampsia is a common cause of maternal and perinatal morbidity and mortality, especially when it occurs early. Although understanding of the pathogenesis of preeclampsia is not entirely clear, the present theory explains its emergence in two stages. The **first stage** is caused by weakened invasion by the trophoblast, resulting in inadequate reshaping of the spiral arteries. It is assumed that this leads to the **second stage**, which involves the **mother's response to the endothelial dysfunction and imbalance between angiogenic and antiangiogenic factors**, which is manifested by the clinical symptoms of the disease. Prediction of the occurrence of preeclampsia in the first trimester of pregnancy is driven by the desire to identify pregnant women with a high risk of developing preeclampsia, which would allow taking necessary measures early enough to improve placentation, prevent disease, or at least to reduce its frequency. Preeclampsia is a gestational disorder, i.e. a syndrome, that is defined by **systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, measured at least twice in a timeframe of 4 hours apart in previously normotensive pregnant women, with the presence of proteinuria of ≥0.3g/L in a 24-hour period urine sample**.

Table 1. Symptoms of severe preeclampsia

• Blood pressure ≥160 and/or 110 mmHg, if measured twice within 4 hours while the pregnant woman is lying down
• Proteinuria ≥0.3g/L/24-hour urine
• Oliguria (500 mL or less in 24 hours)
• Headache or impaired vision
• Epigastric pain
• Pulmonary oedema or cyanosis
• Thrombocytopenia
• Creatinine >9 μmol/L
• Transaminases >40 IU/L
• DIC
• IUGR
• Early onset of preeclampsia, before 34 weeks of gestation, is associated with a high risk of short-term and long-term maternal and perinatal morbidity.
• Late onset of preeclampsia is defined by onset after the 34th week of pregnancy

Risk assessment guidelines for the first trimester of pregnancy

Risk assessment for the development of preeclampsia (between the 11th and 14th week of pregnancy) is suggested in case of identification of 1 major* or 2 moderate** risk factors

Risk assessment includes:

- Family, personal and obstetric history of the pregnant woman
- Physical exam of the pregnant woman (age, body height, body mass, body mass index, blood pressure, mean arterial pressure)
- Pulsatile index of the uterine artery
- Biomarker PlGF

The values are then entered into the FMF algorithm to assess the risk of developing preeclampsia (or any other, accredited preeclampsia risk assessment algorithm) (https://fetalmedicine.org/research/assess/preeclampsia/first-trimester) and, in case of a risk greater than 1:100, to consider the introduction of prophylactic aspirin therapy***

Table 2. Group of high-risk pregnant women for the development of preeclampsia

• Hypertensive disease during previous pregnancy and associated complications (HELLP syndrome, placental abruption, IUGR, stillbirth)
• Chronic hypertension
• Chronic kidney disease
• Autoimmune diseases such as systemic lupus erythematosus
• Acquired thrombophilia (antiphospholipid syndrome)#
• Hereditary thrombophilia (mutation of the prothrombin or factor V gene, deficiency of AT, protein C and protein S)
• Type 1 and type 2 diabetes

Table 3. Group of pregnant women at moderate risk for the development of preeclampsia

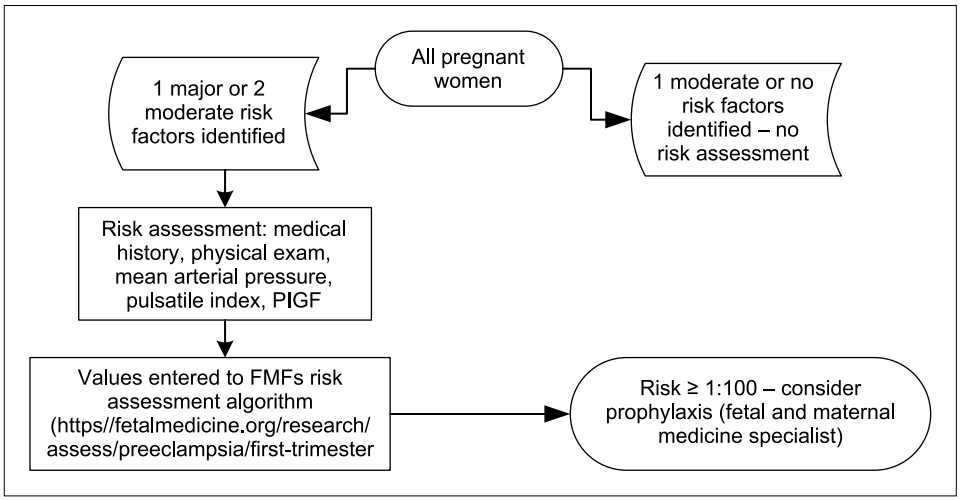
• First pregnancy
• Pregnant age >40 years
• Time interval between two pregnancies >10 years
• Body mass index >35 kg/m^2
• Gestational diabetes
• Family history of preeclampsia
• Twin pregnancy
• Pregnancy after in vitro fertilisation

* High-risk group of pregnant women for the development of preeclampsia

** Group of pregnant women at moderate risk for the development of preeclampsia

*** Prophylactic therapy is indicated by a specialist in fetal and maternal medicine

\# In case of a diagnosis of antiphospholipid syndrome, suggested therapy includes aspirin and heparin



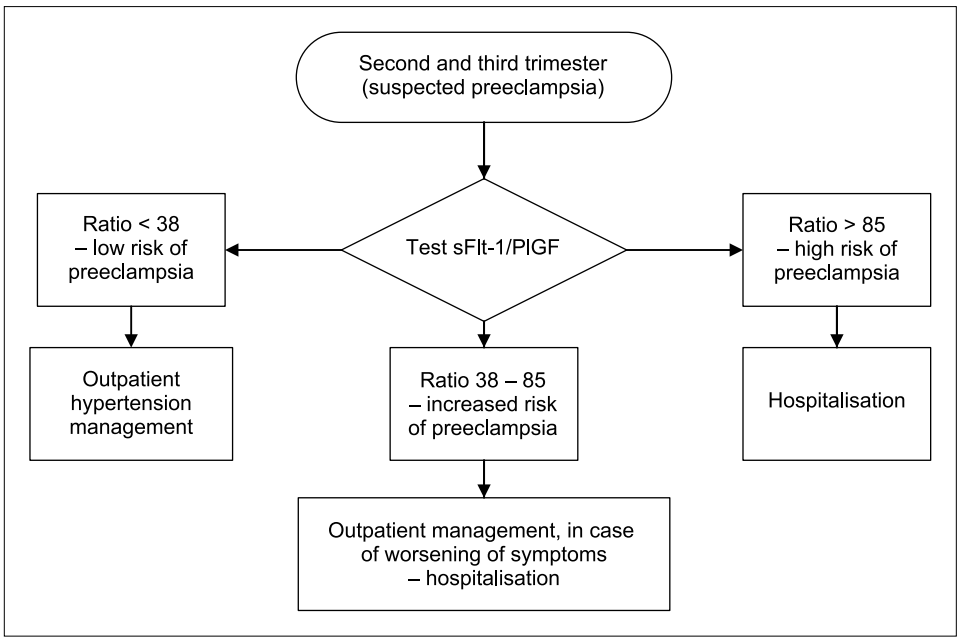
Scheme 1. Guidelines for risk assessment of preeclampsia for the first trimester of pregnancy

Risk assessment guidelines for the second and third trimesters of pregnancy

After the 20th week of pregnancy, use of **sFlt-1/PlGF ratio** is recommended for the purpose of risk assessment for development of preeclampsia, which, in addition to clinical evaluation, may help in predicting or excluding the occurrence of preeclampsia.

To predict the early onset of preeclampsia (weeks 20 to 34) within 4 weeks, threshold values for Elecsys sFlt-1/PlGF are between 38 and 85, and values >85 indicate the early development of preeclampsia.

To predict late preeclampsia (after week 34) within 4 weeks, values for Elecsys sFlt-1/PlGF are between 38 and 110, and values >110 implicate the late development of preeclampsia.



Scheme 2. Guidelines for risk assessment of preeclampsia for the second and third trimesters