Arh. farm. 2025; 75: 84 – 100 *Original scientific paper/Originalni naučni rad*

Association Between Systemic Inflammation and Lipid Metabolism in the Development of Preeclampsia

Tamara Gojković[1*], Daniela Ardalić[2], Gorica Banjac[2], Jelena Vekić[1], Aleksandra Zeljković[1], Jelena Munjas[1], Milica Miljković-Trailović[1], Snežana Jovičić[1], Marija Sarić Matutinović[1], Vesna Spasojević-Kalimanovska[1], Željko Miković[2,3] and Aleksandra Stefanović[1]

[1]Department of Medical Biochemistry, Faculty of Pharmacy, University of Belgrade, Serbia

[2]Gynecology and Obstetrics Clinic Narodni Front, Belgrade, Serbia

[3]Department of Gynecology and Obstetrics, Faculty of Medicine, University of Belgrade, Serbia

*Corresponding author: Tamara Gojković, e-mail: tgojkovic@pharmacy.bg.ac.rs

Received: 21 December 2024; Revised in revised forme: 4 February 2025; Accepted: 6 February 2025

Abstract

Preeclampsia (PE) is a pregnancy complication marked by hypertension (≥ 140/90 mmHg) and proteinuria (≥ 300 mg/24 h), with an unclear pathogenesis involving inflammation and dyslipidemia. This study aimed to longitudinally examine changes in lipid status parameters and inflammatory markers in pregnant women at high risk for PE and those who developed PE. Among 91 women, 20 developed PE (PE group), and 71 were high-risk (HR group). Both groups were monitored at four points: T1-first, T2-, T3-third trimester, and T4-pre-delivery. Lipid markers (triglycerides (TG), total cholesterol (TC), HDL-C, LDL-C, apolipoproteins A-I and B-100) and inflammatory markers (high-sensitivity C-reactive protein (hsCRP), resistin, serum amyloid A (SAA), and macrophage chemotactic protein-1 (MCP-1)) were assessed. Results showed significantly higher TG, resistin, and MCP-1 concentrations in the PE group compared to the HR group at T1 ($p < 0.05$, $p < 0.01$, $p < 0.01$, respectively). During pregnancy, both groups exhibited increases in TG, TC, LDL-C, SAA, and MCP-1 ($p < 0.001$), while HDL-C and resistin increased only in the HR group ($p < 0.001$). PE development is associated with atherogenic lipid changes, characterized by hypertriglyceridemia and no increase in HDL-C, with elevated SAA potentially diminishing HDL's protective role.

Key words: preeclampsia, high-risk pregnancy, lipid profile, inflamation

https://doi.org/10.5937/arhfarm75-55585

Introduction

Pregnancy induces numerous anatomical and physiological changes in a woman's body, including hormonal and metabolic alterations to support fetal development, maintain maternal energy balance, and prepare for childbirth (1). The postpartum effects of these changes are minimal in most women (1). Inadequate maternal metabolic adaptability, which could be similar to metabolic changes in cardiometabolic diseases, could lead to the onset and progression of pregnancy complications (1, 2). Understanding these changes and promptly identifying pregnancy-specific metabolic disorders is crucial for reducing the prevalence of complications and ensuring better long-term health outcomes for both the mother and the child (1, 2).

Preeclampsia (PE) is a severe pregnancy-related complication defined by *de novo* hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) diagnosed after 20 weeks of gestation, accompanied by proteinuria (≥ 300 mg/24 h) and/or signs of other organ damage. Early-onset PE, developing before the 34th week of gestation, is predominantly caused by placental abnormalities, while late-onset PE (developing after 34 weeks of gestation) is more frequently associated with pregnancy comorbidities, such as chronic hypertension, diabetes and obesity, often accompanied by dyslipidemia (2). Physiologically, early pregnancy is marked by shifts in lipid metabolism favoring anabolic processes, resulting in increased lipid synthesis and storage within adipocytes. In the third trimester, lipid metabolism shifts to a catabolic state, increasing lipolysis and releasing fatty acids, which are then utilized in the metabolic processes of the feto-placental unit to support the fetus's rapid growth (3, 4). During pregnancy, lipid metabolism undergoes significant physiological changes, marked by a roughly 50% rise in total cholesterol (TC), a 2–3-fold increase in triglycerides (TG), and a moderate elevation in low-density lipoprotein cholesterol (LDL-C) levels (3). High-density lipoprotein cholesterol (HDL-C) levels also rise by up to 25%, during mid-gestation, exhibiting a slight decrease towards the end of pregnancy (5, 6). HDL functionality extends beyond reverse cholesterol transport, with growing recognition of its anti-inflammatory, antioxidative, antiapoptotic, anti-adhesive, and antithrombotic roles, particularly in conditions of low-grade inflammation such as pregnancy (6). Inadequate placentalization, placental tissue senescence, and risk factors for PE development, such as gestational diabetes and obesity, result in intensive inflammatory cytokine production and an enhanced inflammatory response (2). A widely used clinical biomarker of low-grade inflammation is the high-sensitivity C-reactive protein (hsCRP) (7). In addition to hsCRP, serum amyloid A (SSA) concentration can increase up to 1000 times during the acute-phase response, making it a highly sensitive reactant of the acute phase (8). SSA is synthesized in the liver as a poorly soluble protein, and transported through the circulation as an apolipoprotein of HDL particles (8, 9). It replaces apolipoprotein A-I (apo A-I) from HDL, which could modify HDL functionality (8). Although HDL function is widely recognized to be compromised during inflammation, the specific contribution of SAA to this impairment remains uncertain (9). Further animal model studies have shown that SSA mediates in the macrophage

chemotactic protein-1 (MCP-1) released by vascular smooth muscle cells (10). MCP-1 plays a significant role in the infiltration of monocytes and macrophages during both physiological and pathological conditions (11). Activated macrophages produce inflammatory cytokines, including a cytokine resistin, which plays a pivotal role in inflammation, which is present in PE (12). The majority of resistin in the maternal circulation during pregnancy comes from the placenta (12).

Although inflammation and dyslipidemia in pregnancy have been the focus of previous research, longitudinal changes in the concentrations of resistin, MCP-1 and SAA in high-risk pregnancy and during the development of PE, as well as their relationship with changes in concentrations of lipid status parameters, especially HDL-C, are still incompletely understood. This study aimed to examine longitudinal changes in the concentrations of proinflammatory cytokines and basic lipid profile parameters in high-risk pregnancies and PE. In addition, we aimed to examine the inflammation status during the 1st trimester of high-risk pregnancies. Finally, the study aimed to investigate the development of dyslipidemia during pregnancies in which the development of PE occurs, with special attention to changes in HDL-C concentrations, and to determine the relationship between changes in concentrations of proinflammatory cytokine and lipid status parameters.

Materials and Methods

Study design and patients

This longitudinal observational study was part of a larger research project (HIgh-density lipoprotein MetabolOMe research to improve pregnancy outcome—HI-MOM). This study included pregnant women identified as being at risk for preeclampsia (PE) development during their first antenatal visit to a primary healthcare facility. The pregnant women were referred to a tertiary care facility, Narodni Front Gynecological and Obstetrics Clinic in Belgrade, Serbia, where they were screened for PE. Screening was conducted in the first trimester, between 11 weeks 0 days and 13 weeks 6 days of gestation, to enable early identification of women at heightened risk for developing PE. The screening followed the guidelines issued by the National Institute for Health and Care Excellence (NICE) (13), which classify women as high-risk if they exhibit one high-risk factor or at least two moderate-risk factors. High-risk factors include chronic hypertension, a history of hypertensive disease in a previous pregnancy, chronic kidney disease, diabetes mellitus, or autoimmune diseases. Moderate-risk factors encompass maternal age over 40 years, a first pregnancy, a pregnancy interval exceeding 10 years, body mass index (BMI) of 30 kg/m^2 or higher at the initial visit, and a family history of preeclampsia. The exclusion criteria comprised multifetal pregnancies, miscarriages, abortions, infectious diseases, exacerbations of pre-existing autoimmune conditions at any stage of pregnancy, and a history of malignant disease prior to pregnancy. The study primarily focused on PE as the primary outcome, but it also tracked secondary outcomes such as hypertensive disorders of pregnancy (gestational hypertension and superimposed preeclampsia), intrauterine growth restriction (IUGR), and gestational diabetes mellitus (GDM). Outcomes were defined based

on current guidelines and recommendations (14, 15). The research adhered to the ethical principles outlined in the Declaration of Helsinki, with all participants providing written informed consent. Finally, we monitored 91 pregnant women at risk for PE development. Twenty developed PE (10 had only preeclampsia, while 4 had PE and IUGR, and 6 were diagnosed with PE and gestational diabetes). Nine pregnant women had pregnancy-induced hypertension, 5 only had IUGR, 4 had GDM, 2 had both pregnancy-induced hypertension and gestational diabetes, and 2 had IUGR and GDM. One woman had pregnancy-induced hypertension, GDM, and IUGR, while one had type I diabetes, and 3 had had type II diabetes pre-pregnancy. They were followed longitudinally at 4 time points throughout their pregnancy: first (11–14 weeks of gestation), second (22–25 weeks of gestation), third (28–32 weeks of gestation) trimester, and immediately prior to delivery. Among the high-risk participants, 47 experienced uncomplicated deliveries. Seventy-one pregnant women at risk who did not develop PE were classified as the HR group. Venous blood samples were obtained after a 12 h fasting period using EDTA or serum sample vacuum tubes (Becton, Dickinson and Company, New Jersey, United States). Plasma and serum were isolated through centrifugation at 1500 × g for 10 minutes at a temperature of 4 °C. Portions of each sample were aliquoted and preserved at −80 °C until further analysis.

Clinical and Laboratory analyses

A standard procedure was employed to measure arterial blood pressure, and the mean arterial pressure (MAP) was calculated (16). Concentrations of glucose, urea, hsCRP and parameters of lipid status (TC, HDL-C, TG, apolipoprotein A-I, and apolipoprotein B-100), as well as the activity of the enzyme lactate dehydrogenase (LDH), were determined using an AU480 Beckman autoanalyzer employing routine commercial kits (Beckman, Brea, CA, USA). LDL-C concentration was calculated using the Friedwald equation in samples in which TG concentrations were lower than 4.5 mmol/L. In samples in which TG concentrations were equal to or greater than 4.5 mmol/L (17), a commercial kit (Beckman, Brea, CA, USA) was used to determine the concentration of LDL-C on an AU480 Beckman analyzer. Non-HDL-C was calculated using the formula: TC-LDL-C (18). The concentrations of specific proteins were determined using enzyme-linked immunosorbent assay (ELISA) tests. SAA concentrations were quantified using a commercial Human SAA ELISA Kit (FineTest Biotech Inc., Wuhan, Hubei, China) with intra-assay < 6.4% and inter-assay < 9.9% coefficients of variance. Concentrations of MCP-1 proteins were quantified using a Human MCP-1 ELISA Kit (Wuhan Fine Biotech Co, Wuhan, China) with intra-assay < 7.9% and inter-assay < 12.5% coefficients of variance. Resistin quantification was determined using the Human Resistin ELISA development kit, Duo Set (DY1990, R&D Systems, Abingdon, UK/Minneapolis, USA) with intra-assay < 6%, and inter-assay coefficient of variation was < 10%.

Statistical analysis

Data analysis was performed using the IBM® SPSS® Statistics version 22 software. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to assess data distribution.

Continuous variables with a normal distribution are presented as mean ± standard deviation. Asymmetrically distributed variables were shown as median (interquartile range). Continuous variables were compared using the Student's t-test and Mann-Whitney U tests when two groups of data were compared. When the values of continuous variables of more than two groups of data were compared, repeated measures ANOVA with LSD post hoc tests and the Friedman test with Wilcoxon post hoc tests were used. Categorical variables were presented as relative or absolute frequencies and compared using χ^2 tests. Spearman's rank correlation analysis was used to assess univariate associations between lipid and inflammatory parameters, followed by multiple regression analysis to estimate the independent contribution of the predictors to the variance in HDL-C levels. A p-value below 0.05 was regarded as statistically significant.

Results

Table I summarizes the general characteristics of the examined groups. Participants were matched by age. No differences were found in the maternal smoking status before pregnancy or in pregestational supplementation (Table I). Women who developed PE during pregnancy had significantly higher BMI values before pregnancy than the HR group ($p < 0.05$). MAP was significantly higher in the PE group compared with HR ($p < 0.05$).

Table I General characteristics of study groups
Tabela I Osnovne karakteristike ispitivanih grupa

Parameters	**HR (*n* = 71)**	**PE (*n* = 20)**	***p***
Age, years	32±5.6	33±4.2	0.394
Pregestational BMI, kg/m2#	22.7 (20.4–26.6)	25.9 (23.0–29.9)	**< 0.05**
Pregestational vitamin supplementation, n (%)*	59 (83.1)	16 (80)	0.728
Pregestational smoking, *n* (%)*	21 (29.2)	9 (45.0)	0.286
MAP, mmHg	86±11.6	92±9.0	**< 0.05**
Pregnancy weight gain, kg	3.6±2.55	4.1±2.92	0.506

BMI – body mass index; MAP – mean arterial pressure. Data are expressed as mean ± standard deviation for normally distributed parameters. #Data are shown as median and interquartile range for non-normally distributed parameters. Continuous variables were compared using the Student's t-test and Mann-Whitney U tests. *Data are presented as absolute and relative frequencies and compared using χ2-test. Bold values indicate statistical significance.

Longitudinal changes in lipid status parameters and inflammatory markers in the HR group across four time points during pregnancy are presented in Table II. TC levels significantly increased from T1 to T2 ($p < 0.001$), peaking in T3 and T4, with a significant difference compared to T1 ($p < 0.001$ for both), as well as compared to T2 ($p < 0.001$ for both). Concentrations of HDL-C followed a similar trend, increasing significantly in the T2–T4 period. In all three points, the values were significantly higher compared to T1 ($p < 0.001$, $p < 0.001$, $p < 0.01$, respectively). LDL-C concentrations rose progressively ($p < 0.001$, in all points compared to T1), reaching a peak in T3 and then declining slightly

at T4. Concentrations of TG demonstrated a continuous and significant increase, with significant differences observed across all trimesters ($p < 0.001$). Differences between all points were also observed in non-HDL-C, and apo B-100, whose levels increased during pregnancy ($p < 0.001$ for all parameters). Concentrations of apo A-I were increased throughout pregnancy compared to T1 ($p < 0.001$, in all points). Among the inflammatory markers, hsCRP levels did not show statistically significant changes ($p = 0.234$). Resistin concentrations significantly increased from T1, maintaining high values until the end of pregnancy ($p < 0.001$, in all points compared to T1). A significant increase in SAA concentrations was observed in T2. These values in T3 were higher compared to the other observed points ($p < 0.001$, in all points compared to T3). MCP-1 concentrations change as pregnancy progresses following the curvilinear pattern, with the highest values in T1 and T3 points ($p < 0.001$, compared to T2 and T4). As expected, there were changes in glucose concentration ($p < 0.001$), as well as an increase in uric acid concentration and LDH activity during the pregnancy ($p < 0.001$).

Table II Basic biochemical parameters, extended lipid profile, and inflammatory markers in the HR group across trimesters of pregnancy

Tabela II Osnovni biohemijski parametri, parametri proširenog lipidnog profila i inflamatorni markeri u HR grupi kroz trimestre tokom trudnoće

Parameters	T1	T2	T3	T4	p
Glucose, mmol/L[#]	4.6 (4.4–4.9)	4.5 (4.2–4.8)^{a**}	4.4 (4.6–4.9) ^{b**}	4.4 (4.1–4.7) ^{a***,c***}	**< 0.001**
TC, mmol/L	5.3±1.08	6.8±1.37 ^{a***}	7.3±1.50 ^{a***,b***}	7.5±1.61 ^{a***,b***}	**< 0.001**
HDL-C, mmol/L	1.8±0.34	2.1±0.39 ^{a***}	2.0±0.44 ^{a***} ^{b**}	2.0±0.52 ^{a**,b**}	**< 0.001**
LDL-C, mmol/L	2.9±0.86	3.8±1.15 ^{a***}	4.2±1.25 ^{a***,b***}	4.1±1.28 ^{a***} ^{b*}	**< 0.001**
TG, mmol/L[#]	1.29 (1.04–1.55)	1.88 (1.55–2.27) ^{a***}	2.3 (1.81–2.95) ^{a***,b***}	2.95 (2.39–3.65) ^{a***,b***,c***}	**< 0.001**
Non-HDL, mmol/L	3.6±0.95	4.7±1.19 ^{a***}	5.3±1.32 ^{a***,b***}	5.5±1.41 ^{a***,b***} ^{c*}	**< 0.001**
Apo B-100, g/L	1.02±0.253	1.34±0.316 ^{a***}	1.48±0.371 ^{a***,b***}	1.54±0.395 ^{a***,b***c*}	**< 0.001**
Apo A-I, g/L[#]	1.93 (1.66–2.20)	2.31 (2.06–2.58) ^{a***}	2.31 (1.97–2.54) ^{a***}	2.24 (1.95–2.46) ^{a***b*}	**< 0.001**
Uric acid, μmol/L	190±35.6	208±35.8 ^{a***}	216±39.3 ^{a***} ^{b**}	262±55.5 ^{a***,b***,c***}	**< 0.001**
LDH, IU/L	135 (120–149)	139 (129–158) ^{a**}	145 (131–157) ^{a***}	156 (139–174) ^{a***,b***,c***}	**< 0.001**
hsCRP, mg/L[#]	3.8 (2.5–8.7)	4.7 (2.9–8.0)	3.8 (2.4-6.6)	4.3 (2.2–8.4)	0.234
Resistin, ng/mL	22.4±8.01	37.3±17.55 ^{a***}	32.7±13.63 ^{a***} ^{b**}	34.5±16.75 ^{a***}	**< 0.001**
SAA, ng/mL[#]	32.8 (16.4–50.1)	42.0 (28.3–69.5) ^{a***}	128.7 (95.3–161.6) ^{a***,b***}	24.6 (12.6–50.3) ^{b***,c***}	**< 0.001**
MCP-1, pg/mL[#]	215.6 (172.4–296.8)	150.1 (109.6–209.2) ^{a***}	228.0 (174.2–322.7) ^{b***}	178.0 (139.6–214.1) ^{a***,c***} ^{b**}	**< 0.001**

TC – total cholesterol; TG – triglyceride; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; Apo – Apolipoprotein; hs-CRP – high sensitivity C-reactive protein; SAA – Serum amyloid A; MCP-1 – Monocyte chemoattractant protein-1. Data are expressed as mean ± standard deviation for normally distributed parameters. [#]Data shown as median and interquartile range for non-normally distributed parameters. Continuous variables were compared using repeated measures ANOVA and the Friedman test with LSD and Wilcoxon post hoc tests, respectively. [a] – significantly different from the first trimester; [b] – significantly different from the second trimester; [c] – significantly different from the third trimester. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. Bold values indicate statistical significance.

The same statistical analysis was conducted in the group of pregnant women who developed PE. The data are presented in Table III. TC concentrations increased during pregnancy and differed significantly compared to T1 ($p < 0.001$). TG concentrations also increased during pregnancy, with a statistically significant increase observed at each time point ($p < 0.001$). The concentrations of HDL-C, glucose, hsCRP and resistin did not change significantly during the entire observation period (Table III). The same pattern of changes was observed for SAA and MCP-1 in the PE group as in the HR group. SAA levels peaked at T3, significantly differing from T1 ($p < 0.001$), T2 ($p < 0.01$), and T4 ($p < 0.001$), while MCP-1 concentrations showed a curvilinear pattern of changes ($p < 0.001$). The highest values of MCP-1 concentrations were observed in T1 and T3. Concentrations of non-HDL-C, apo B-100, and apo A-I exhibited a significant increase during pregnancy ($p < 0.001$), as well as urea concentrations ($p < 0.01$), and LDH activity ($p < 0.05$).

Table III Basic biochemical parameters, extended lipid profile, and inflammatory markers in the PE group across trimesters of pregnancy

Tabela III Osnovni biohemijski parametri, parametri proširenog lipidnog profila i inflamatorni markeri u PE grupi kroz trimestre tokom trudnoće

Parameters	T1	T2	T3	T4	p
Glucose, mmol/L#	4.8 (4.5–5.4)	4.8 (4.4–5.3)	4.9 (4.5–5.4)	4.7 (4.3–5.1) ^{c*}	0.298
TC, mmol/L	5.4±0.76	6.6±1.24 ^{a***}	7.0±1.41 $^{a*** b*}$	7.2±1.51 $^{a*** b**}$	**< 0.001**
HDL-C, mmol/L	1.9±0.61	1.9±0.37	2.0±0.68	1.9±0.31	0.959
LDL-C, mmol/L	2.8±0.66	3.5±1.12 ^{a**}	3.5±1.31 ^{a**}	3.5±1.65 ^{a*}	**< 0.01**
TG, mmol/L#	1.61 (1.19–1.97)	2.38 (1.75–2.92) ^{a***}	2.75 (2.21–3.66) $^{a*** b**}$	3.62 (2.78–4.61) ^{a***,b***c**}	**< 0.001**
Non-HDL, mmol/L	3.6±0.58	4.7±1.14 ^{a***}	4.9±1.25 ^{a***}	5.2±1.50 $^{a*** b*}$	**< 0.001**
Apo B-100, g/L	1.08±0.252	1.29±0.300 ^{a***}	1.36±0,345 ^{a***}	1.53±0.455 $^{a*** b**,c**}$	**< 0.001**
Apo A-I, g/L#	1.84 (1.65–2.39)	2.27 (1.95–2.68) ^{a**}	2.26 (2.01–2.53) ^{a**}	2.30 (2.02–2.67) ^{a**}	**< 0.001**
Uric acid, μmol/L	222±41.4	234±40.3	255±47.7 ^{a**,b**}	302±73.8 ^{a***,b***,c***}	**< 0.01**
LDH, IU/L	131 (119–147)	131 (112–148)	134 (121–155)	146 (115–168) ^{b*}	**< 0.05**
hsCRP, mg/L#	5.2 (3.0–7.7)	5.6 (3.8–8.4)	5.4 (3.6–9.8)	5.0 (3.0–6.2)	0.222
Resistin, ng/mL	31.1±11.71	38.0±16.6	31.9±11.98	34.1±16.65	0.375
SAA, ng/mL#	25.8 (8.8–59.6)	32.2 (15.0–60.6)	113.3 (90.4–134.8) $^{a*** b**}$	19.7 (8.0–59.5) ^{c***}	**< 0.001**
MCP-1, pg/mL#	369.9 (234.3–407.1)	197.1 (122.4–255.8) ^{a***}	292.4 (237.1–373.7) ^{b**}	269.1 (186.4–387.0) $^{a** b*,c*}$	**< 0.001**

TC – total cholesterol; TG – triglyceride; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; Apo – Apolipoprotein; hs-CRP – high sensitivity C-reactive protein; SAA – Serum amyloid A; MCP-1 – Monocyte chemoattractant protein-1. Data are expressed as mean ± standard deviation for normally distributed parameters. #Data shown as median and interquartile range for non-normally distributed parameters. Continuous variables were compared using repeated measures ANOVA and Friedman test with LSD and Wilcoxon post hoc tests, respectively. a – significantly different from the first trimester; b – significantly different from the second trimester; c – significantly different from the third trimester; d – significantly different from the fourth trimester. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. Bold values indicate statistical significance.

We further compared the concentrations of inflammatory markers and lipid status parameters between the groups at T1 to assess whether differences were present at the beginning of pregnancy. Resistin and MCP-1 concentrations were significantly higher in T1 among pregnant women who subsequently developed PE ($p < 0.01$ for both). No significant

differences in hsCRP concentrations were observed between the groups ($p = 0.304$). Among the lipid status parameters, only TG concentrations were significantly higher in the group of pregnant women with PE ($p < 0.05$). TG and MCP-1 concentrations were compared using Mann-Whitney U tests, while SAA concentrations were compared using the Student's t-test.

A correlation analysis was conducted to investigate the possible association between inflammatory markers and lipid status parameters (Table IV). In the HR group, a significant positive correlation was observed between resistin levels and TC concentrations ($r = 0.468$, $p < 0.001$), LDL-C concentrations ($r = 0.534$, $p < 0.001$), as well as concentrations of apo B-100 ($r = 0.364$, $p < 0.01$) and non-HDL-C ($r = 0.506$, $p < 0.001$) at T1. Additionally, at T2 and T3, resistin concentrations were in a significant positive correlation with TG concentrations ($r = 0.243$, $p < 0.05$, $r = 0.249$, $p < 0.05$, respectively). In the HR group, at T1, SAA levels were negatively correlated with HDL-C ($r = -0.250$, $p < 0.05$) and apo A-I concentrations ($r = -0.233$, $p < 0.05$). In the same study group, MCP-1 levels exhibited a negative correlation with TG concentrations at T2 ($r = -0.267$, $p < 0.05$), while hsCRP values showed a negative correlation with HDL-C levels at T3 ($r = -0.254$, $p < 0.05$). In the PE group, resistin concentrations showed a positive correlation with LDL-C concentrations at T1 ($r = 0.598$, $p < 0.01$). Additionally, at T3, a positive correlation was observed between SAA concentrations and HDL-C levels ($r = 0.535$, $p < 0.05$).

In addition, we performed multiple regression analysis to assess the confounding effects of BMI, gestational week (GW), and inflammatory parameters that showed significant correlations with HDL-C concentrations in Spearman's nonparametric correlation analysis (Table IV). In the multiple regression analysis, BMI, GW, and inflammatory markers (SAA, hsCRP, and SAA in the HR group at T1, T3, and PE group at T3, respectively) were factors that independently influenced HDL-C concentration (Table V). In the multiple regression analysis, SAA ($p < 0.01$) and GW (< 0.05) were factors that showed an independent influence on HDL-C concentrations.

Table IV Correlations between inflammatory parameters and extended lipid profile during pregnancy in both studied groups

Tabela IV Korelacije između inflamatornih markera i parametara proširenog lipidnog profila tokom trudnoće u obe ispitivane grupe

			TC, mmol/L	TG, mmol/L	HDL –C, mmol/L	LDL-C, mmol/L	Apo B-100 (g/L)	Apo A- I, g/L	Non-HDL, mmol/L
HR group	T1	Resistin, ng/ml	0.468***			0.534***	0.364**		0.506***
		SAA, ng/mL			-0.250*			-0.233*	
	T2	Resistin, ng/ml		0.243*					
		MCP-1, pg/mL		-0.267*					
	T3	hsCRP, mg/L			-0.254*				
		Resistin, ng/ml		0.249*					
PE group	T1	Resistin, ng/ml				0.598**			
	T3	SAA, ng/mL			0.535*				

TC – total cholesterol; TG – triglyceride; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; Apo – Apolipoprotein; hs-CRP - high sensitivity C-reactive protein; SAA – Serum amyloid A; MCP-1 – Monocyte chemoattractant protein-1. Data are expressed as the Spearman's rank correlation coefficient. $^{*}p < 0.05$, $^{**}p < 0.001$. $^{***}p < 0.001$.

Table V Multiple linear regression analysis for the predictors of HDL-C concentration

Tabela V Multipla linearna regresiona analiza prediktora koncentracije HDL-H

		Predictors for HDL, mmol/L Adjusted R2 = 0.106	B (95% CI)	SE	p
HR group	T1	SAA, ng/mL	-0.005 (-0.008–-0.002)	0.001	**< 0.01**
		GW, weeks + days	0.033 (-0.064–0.129)	0.048	0.503
		BMI, kg/m^2	-0.003 (-0.019–0.013)	0.008	0.712
		Predictors for HDL, mmol/L Adjusted R2 = -0.008	**B (95% CI)**	**SE**	**p**
	T3	hsCRP, mg/L	-0.007 (-0.019–0.006)	0.006	0.290
		GW, weeks + days	0.080 (-0.063–0.223)	0.072	0.268
		BMI, kg/m^2	-0.003 (-0.019–0.013)	0.008	0.712
PE group		**Predictors for HDL, mmol/L Adjusted R2 = 0.372**	**B (95% CI)**	**SE**	**p**
	T3	SAA, ng/mL	0.003 (-0.001–0.007)	0.002	0.091
		GW, weeks + days	0.149 (0.008–0.290)	0.066	**< 0.05**
		BMI, kg/m^2	-0.024 (-0.059–0.010)	0.016	0.155

HDL-C – high-density lipoprotein cholesterol; SAA – Serum amyloid A; hs-CRP – high sensitivity C-reactive protein; GW – gestational week; BMI – Body mass index; SE – standard error. Data are expressed as coefficients (B) with 95% confidence intervals (CI). $^{*}p < 0.05$, $^{**}p < 0.01$. $^{***}p < 0.001$.

Discusion

In this study, we examined the changes in concentrations of inflammatory markers and basic lipid status parameters in HR pregnancies, with special reference to PE. We intended to emphasize the importance of a comprehensive and in-depth investigation into the molecular interplay between inflammation and dyslipidemia in the pathogenesis of PE development. PE management has made limited advances over time, possibly because of the slow progress in understanding its pathology. Effective strategies for addressing PE can be categorized into three key areas: prevention, early detection, and treatment (19). Identifying women who are at a higher risk of developing PE at an early stage represents a fundamental aspect of effective management, as recommended by the NICE (13). Our results show that obesity is an important risk factor for the occurrence of PE. Pregnant women who developed PE had a significantly higher pre-pregnancy BMI compared to the HR group (Table I). This observation highlights that maternal overweight before pregnancy significantly elevates the risk of metabolic complications during gestation, emphasizing the critical role of pre-pregnancy metabolic health in achieving favorable pregnancy outcomes. Numerous studies have sought to develop an effective model for predicting PE using available clinical data and easily measurable biochemical parameters (20). Most of these models include MAP as one of the readily available clinical parameters (20, 21). In a study by Mayrink et al. involving 1,165 pregnant women, MAP was used as an isolated marker for PE prediction (21). The results showed that women with early onset PE at 20 weeks of gestation had elevated MAP levels compared to the normotensive group (21). Our results confirm these findings, as the results from our cohort revealed significantly higher MAP values in the PE group as early as in the first trimester (Table I). During pregnancy, changes in lipid status parameters are hormonally regulated to support the proper growth and development of the fetus (6). Estrogen plays a key role by acting on hepatocytes to increase the production of very-low-density lipoprotein (VLDL) particles, primarily through the upregulation of apolipoprotein B gene expression, a critical component of VLDL. This process leads to an increased synthesis of endogenous TG. Elevated TG concentrations may induce the remodeling of HDL lipoprotein particles, a process controlled by the cholesteryl ester transfer protein (CETP), whose expression is upregulated by estrogen (6). These results emphasize the need for a more comprehensive understanding of lipoprotein metabolism during pregnancy, particularly the metabolism of HDL particles. In this study, we confirmed the results of previous studies that described changes in the concentrations of basic lipid status parameters during pregnancy (Table II and Table III). A significant increase in TC concentrations was observed in both groups during pregnancy. These changes were accompanied by an increase in LDL-C concentrations, which was maintained in the HR group throughout pregnancy. Studies have shown that LDL concentrations increase steadily during pregnancy, while HDL concentrations peak in the second trimester and decrease slightly towards the end of pregnancy (5, 22). This pattern of changes in HDL-C concentrations suggests the importance of gestational age when sampling for lipoprotein analysis, which contributed to the adequate design of this study

and the inclusion of four follow-up time points for data collection (6). Our study results revealed distinct patterns of HDL-C concentration changes between the groups (Table II and Table III). In the HR group, HDL-C levels significantly fluctuated throughout pregnancy, peaking in the second trimester (T2) and maintaining elevated levels until delivery. In contrast, no significant changes in HDL-C concentrations were observed in the group of pregnant women who developed PE throughout the entire follow-up period. The authors suggest that, during physiological pregnancies, the increase in HDL-C levels reflects a higher proportion of HDL lipoprotein particles with significant atheroprotective features, which thus in some way protect the pregnancy from cardiometabolic complications development (3, 4–6, 22). However, inadequate changes in HDL-C levels, combined with the low-grade inflammation typical of pregnancy, are associated with the occurrence of complications such as gestational diabetes, PE, and an increased CVD risk later in the mother's life (6, 23, 24). Unlike HDL-C levels, apo A-I concentrations increased significantly during pregnancy in both studied groups (Tables II and III). Estrogen influences the synthesis of apoA, a key protein involved in HDL metabolism, further impacting lipid dynamics during pregnancy. In addition to the liver, apoA can be synthesized by the placenta during pregnancy (25). This has resulted in conflicting findings regarding its role. While apoA is known for its cardioprotective properties, studies have also reported elevated concentrations during pregnancy, which are associated with adverse pregnancy outcomes (25, 26). It can be hypothesized that, in the unfavorable maternal metabolic conditions characteristic of pregnancy complications, apo A-I may undergo structural and functional alterations, potentially losing its antiatherogenic properties. Additionally, TG concentrations showed a significant increase during pregnancy (Tables II and III), aligning with the findings from other studies, which reported that TG levels in the T3 could rise by up to 300% compared to T1 values (27). Our results showed that, among all lipid profile parameters analyzed, only TG concentrations were significantly higher in the PE group compared to the HR group during the first trimester ($p < 0.05$). These results suggest that pre-pregnancy obesity (Table I) and hypertriglyceridemia at the beginning of pregnancy are associated with an increased risk of developing PE. Moreover, hypertriglyceridemia is accompanied by intravascular remodeling of HDL lipoprotein particles mediated by CETP, which diminishes their protective potential (6). Our findings underscore the role of dyslipidemia in BMI-related PE development. Although resistin is recognized for its involvement in the regulation of insulin sensitivity, inflammation, and energy metabolism, its influence on the metabolism during pregnancy remains incompletely understood. Resistin is also highly expressed in macrophages, where it plays a key role in the inflammatory response (12). As a pro-inflammatory cytokine, its effects are primarily mediated through TNFα (28). Nien et al. conducted a study showing that healthy pregnant women have higher median plasma resistin levels than non-pregnant women, with concentrations rising progressively throughout pregnancy (29). This increase in maternal blood resistin was positively associated with gestational age, but not with maternal BMI. The authors suggested that pregnancy-related metabolic changes could be attributed to alterations in

maternal plasma resistin levels and confirmed state of low-grade inflammation during pregnancy (29). In our study, we observed that in the HR group resistin concentrations increased significantly in T2, T3, and T4 compared with T1, with peak levels during the 2nd trimester (Table II). This pattern of trajectory was not observed in the PE group (Table III). However, resistin concentrations in the PE group were significantly higher compared with HR during the first trimester ($p < 0.01$). Additionally, correlation analysis revealed that, in the HR group, resistin levels at the beginning of pregnancy were positively associated with TC, LDL-C, apoB-100, and non-HDL concentrations, and later in pregnancy with TG concentrations. In contrast, in the PE group, resistin concentrations showed a positive correlation only with LDL-C concentrations (Table IV). Previous studies have highlighted the role of resistin in glucose and lipid metabolism during pregnancy and its potential involvement in the development of GDM, where resistin levels were notably elevated in comparison to healthy pregnancies (30). Furthermore, a positive association between maternal and fetal resistin concentrations, as well as its correlation with gestational age, suggests a placental source of resistin or the existence of a resistin placental transporter (12). Our findings suggest that the increased resistin concentrations accompanied by adaptive changes in lipid metabolism observed in the HR group of pregnant women are absent in the PE group, and are accompanied only by changes in LDL-C concentrations. This underscores the need for further research to clarify the role of resistin in metabolic changes and its contribution to the inflammatory cascade during pregnancy. The inflammatory profile in a physiological pregnancy is complex and dynamic. It initially promotes a pro-inflammatory state during placental development, followed by an anti-inflammatory phase that supports maternal tolerance of the maturing semi-allogeneic fetus (6, 31). Our study results demonstrate that MCP-1 concentrations change as pregnancy progresses, with a curvilinear pattern observed in both groups (Table II and Table III). During the 1st trimester, MCP-1 levels were considerably higher in the PE group in comparison to the HR group ($p < 0.01$). As a chemotactic factor, MCP-1 concentrations were significantly elevated in the amniotic fluid and serum of women who experienced preterm birth, indicating that higher MCP-1 levels may be associated with adverse pregnancy outcomes (32). Garcia et al. conducted a study investigating early pregnancy immune biomarkers in peripheral blood that could predict PE. Their logistic regression model revealed that the most accurate predictors were the combination of MCP-1 serum levels, IL-8, and TNFα/IL-10 ratios (33). Elevated concentrations of hsCRP are recognized as being linked to the development of obstetric complications and the severity of hypertensive disorders in pregnancy (34). Some authors recommend the use of hsCRP as a prognostic marker to identify pregnant women at high risk for complications (34, 35). However, we did not find significant changes in hsCRP levels throughout pregnancy in either of the studied groups. Additionally, and somewhat unexpectedly, no differences in hsCRP values were observed between the groups at T1 ($p = 0.304$). This could be attributed to the fact that the pregnant women in this study were already at risk of developing complications and had been in a mild inflammatory state even before pregnancy. Additionally, the reason for the lack of differences in the

concentrations could also lie in the small sample size, the sensitivity of the method, and biological variation. SAA is an acute-phase protein predominantly produced in the liver and released into the bloodstream, where it is incorporated into HDL particles (8, 9). During pregnancy, part of the SAA present in the mother's circulation is also of placental origin (10). Overexpression of the SAA gene during the development of senescence-associated secretory phenotype (SASP) was demonstrated in *in vitro* experiments (36). It has been proven that PE is accompanied by placenta senescence and excessive production of the secretome characterized by SASP (2). Recent evidence suggests that SAA may act as a host-derived damage-associated molecular pattern (DAMP) protein, helping to detect danger signals during pregnancy (37). Our study revealed a gradual increase in SAA concentrations throughout the follow-up of pregnant women in the HR group, reaching peak levels at T3 (Table II). Conversely, in the PE group, a sudden rise in SAA concentrations was observed at T3 (Table III). Notably, in the PE group, SAA concentrations at T3 were positively correlated with HDL-C levels. In contrast, in the HR group during the first trimester, SAA was negatively correlated with HDL-C and apoA-I concentrations, suggesting potential remodeling of the protein composition of HDL particles early in pregnancy (Table IV). Additionally, in the HR group at T1, SAA was identified as an independent factor influencing HDL-C (Table V). Existing evidence indicates that the binding of SAA to HDL reduces the anti-inflammatory role of HDL particles. In contrast, the authors suggest that this coupling likely enhances SSA stability or reduces its pro-inflammatory effects, rather than directly affecting HDL functionality during acute inflammation (9). These findings underscore the complex mechanisms regulating SAA secretion and its influence on HDL particle functionality, highlighting the need for further research in this area.

Conclusion

The results presented in this study suggest the existence of different lipoprotein and inflammatory patterns during high-risk pregnancies and those complicated by the development of PE. Of particular significance are the differing patterns of HDL-C concentration changes observed between the groups, as well as the early manifestation of hypertriglyceridemia in pregnancies that later progressed to PE. Considering the cardioprotective role of HDL particle, favorable adaptive changes in its protein and lipid composition could positively influence pregnancy outcomes. Furthermore, alterations in resistin and SAA concentrations highlight the need for a deeper investigation into the inflammatory cascade in conditions characterized by low-grade inflammation, such as pregnancy. Our findings emphasize the importance of lipid profile parameter quantifications during pregnancy to obtain a comprehensive metabolic assessment and improve risk stratification by identifying women at increased risk of developing PE. This approach may facilitate closer monitoring and timely interventions. Furthermore, understanding the role of these parameters in PE pathophysiology could pave the way for the development of new therapeutic strategies.

A limitation of this study is that, aside from age matching, other potential confounders such as BMI, socioeconomic status, diet, and physical activity levels were not controlled, which may have influenced the observed associations.

Acknowledgements

This research was supported by the Science Fund of the Republic of Serbia [Grant No. 7741659], HIgh-density lipoprotein MetabolOMe research to improve pregnancy outcome–HI-MOM. The authors appreciate the support from the Ministry of Science, Technological Development and Innovation, the Republic of Serbia [Grant Agreement with the University of Belgrade – Faculty of Pharmacy, No. 451-03-65/2024-03/200161 and No. 451-03-66/2024-03/200161].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Tamara Gojković: Conceptualization, Data curation, Formal analysis, Investigation, and Roles/Writing – original draft; Aleksandra Stefanović: Conceptualization, Data curation, Funding acquisition, Project administration, Roles/Writing – original draft; Jelena Vekić, Aleksandra Zeljković, and Željko Miković: Conceptualization, Methodology, Supervision; Daniela Ardalić, Gorica Banjac, Jelena Munjas, Milica Miljković-Trailović, Snežana Jovičić, Marija Saric Matutinović, and Vesna Spasojević-Kalimanovska: Data curation, Formal analysis, Investigation, Methodology.

References

1. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr. 2016;2:89–94.
2. Suvakov S, Kattah AG, Gojkovic T, Enninga EA, Pruett J, Jayachandran M, et al. Impact of aging and cellular senescence in the pathophysiology of preeclampsia. Compr Physiol. 2023;4:5077–114.
3. Wild R, Feingold KR. Effect of pregnancy on lipid metabolism and lipoprotein levels. Endotext [Internet]. 2023 [cited 2024 Dec 15]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK498654/
4. Herrera E, Ortega-Senovilla H. Maternal lipid metabolism during normal pregnancy and its implications to fetal development. Clin Lipidol. 2010;6:899–911.

5. Grantz KL, Elmi A, Pugh SJ, Catov JM, Sjaarda L, Albert PS. Maternal serum lipid trajectories and association with pregnancy loss and length of gestation. Am J Perinatol. 2020;9:914–23.
6. Woollett LA, Catov JM, Jones HN. Roles of maternal HDL during pregnancy. Biochim Biophys Acta Mol Cell Biol Lipids. 2022;3:159–66.
7. Banait T, Wanjari A, Danade V, Banait S, Jain J. Role of high-sensitivity C-reactive protein (Hs-CRP) in non-communicable diseases: a review. Cureus. 2022;10:e29680.
8. Sack Jr GH. Serum amyloid A – a review. Mol Med. 2018;1:46.
9. Webb NR. High-density lipoproteins and serum amyloid A (SAA). Curr Atheroscler Rep. 2021;23:1–8.
10. Schuchardt M, Prüfer N, Tu Y, Herrmann J, Hu XP, Chebli S, et al. Dysfunctional high-density lipoprotein activates toll-like receptors via serum amyloid A in vascular smooth muscle cells. Sci Rep. 2019;9(1):3421.
11. Bardou M, Hadi T, Mace G, Pesant M, Debermont J, Barrichon M, et al. Systemic increase in human maternal circulating CD14+ CD16− MCP-1+ monocytes as a marker of labor. Am J Obstet Gynecol. 2014;1:70.e1.
12. Floeck A, Ferrari N, Joisten C, Puth MT, Strizek B, Dolscheid-Pommerich R, et al. Resistin in pregnancy: analysis of determinants in pairs of umbilical cord blood and maternal serum. Cytokine X. 2021;2:100052.
13. National Institute for Health and Clinical Excellence. Hypertension in pregnancy: the management of hypertensive disorders during pregnancy. NICE; 2010.
14. The American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2019;133:e1-25.
15. Sharma D, Shastri S, Sharma P. Intrauterine growth restriction: antenatal and postnatal aspects. Clin Med Insights Pediatr. 2016;10:67–83.
16. Katz ED, Ruoff BE. Commonly Used Formulas and Calculations. In: Roberts J, Hedges J, editors. Clinical Procedures in Emergency Medicine, 4th ed. Elsevier Mosby Publishing: Philadelphia, PA, USA, 2004; p. 1434.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499–502.
18. Virani SS. Non-HDL cholesterol as a metric of good quality of care: opportunities and challenges. Tex Heart Inst J. 2011;38(2):160.
19. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integr Blood Press Control. 2015;3:7–12.
20. De Kat AC, Hirst J, Woodward M, Kennedy S, Peters SA. Prediction models for preeclampsia: A systematic review. Pregnancy Hypertens. 2019;16:48–66.
21. Mayrink J, Souza RT, Feitosa FE, Rocha Filho EA, Leite DF, Vettorazzi J, et al. Mean arterial blood pressure: potential predictive tool for preeclampsia in a cohort of healthy nulliparous pregnant women. BMC Pregnancy Childbirth. 2019;19:1–8.
22. Mankuta D, Elami-Suzin M, Elhayani A, Vinker S. Lipid profile in consecutive pregnancies. Lipids Health Dis. 2010;9:1–4.

23. Bao W, Dar S, Zhu Y, Wu J, Rawal S, Li S, et al. Plasma concentrations of lipids during pregnancy and the risk of gestational diabetes mellitus: A longitudinal study. J Diabetes. 2018;6:487–95.
24. Sharami SH, Tangestani A, Faraji R, Zahiri Z, Amiri A. Role of dyslipidemia in preeclamptic overweight pregnant women. Iran J Reprod Med. 2012;2:105.
25. Melhem H, Kallol S, Huang X, Lüthi M, Ontsouka CE, Keogh A, et al. Placental secretion of apolipoprotein A1 and E: the anti-atherogenic impact of the placenta. Sci Rep. 2019;1:6225.
26. Gil-Acevedo L, Ceballos G, Torres-Ramos Y. Foetal lipoprotein oxidation and preeclampsia. Lipids Health Dis. 2022;21:51.
27. Diareme M, Karkalousos P, Theodoropoulos G, Strouzas S, Lazanas N. Lipid profile of healthy women during normal pregnancy. J Med Biochem. 2009;3:152–63.
28. Gugliucci A. Biomarkers of dysfunctional visceral fat. Adv Clin Chem. 2022;109:1–30.
29. Nien JK, Mazaki-Tovi S, Romero R, Kusanovic JP, Erez O, Gotsch F, et al. Resistin: a hormone which induces insulin resistance is increased in normal pregnancy. J Perinat Med. 2007;6:513–21.
30. Siddiqui K, George TP. Resistin role in development of gestational diabetes mellitus. Biomarkers Med. 2017;7:579–86.
31. Parisi F, Milazzo R, Savasi VM, Cetin I. Maternal low-grade chronic inflammation and intrauterine programming of health and disease. Int J Mol Sci. 2021;4:1732.
32. Bogavac MA, Ćelić DD, Perić TM. A prospective study of mid-trimester MCP-1 levels as a predictor of preterm delivery. Medicines. 2022;1:7.
33. Garcia MS, Mobley Y, Henson J, Davies M, Skariah A, Dambaeva S, et al. Early pregnancy immune biomarkers in peripheral blood may predict preeclampsia. J Reprod Immunol. 2018;125:25–31.
34. Joshi K, Acharya N, Acharya S, Joshi S. Maternal serum high-sensitivity C-reactive protein (hsCRP) as a prognostic marker of fetomaternal outcome in hypertensive disorders of pregnancy: a novel study. Cureus. 2022;4:1–9.
35. Dhok AJ, Daf S, Mohod K, Kumar S. Role of early second trimester high sensitivity C-reactive protein for prediction of adverse pregnancy outcome. JK Sci. 2011;3:141–4.
36. Ebert R, Benisch P, Krug M, Zeck S, Meißner-Weigl J, Steinert A, et al. Acute phase serum amyloid A induces proinflammatory cytokines and mineralization via toll-like receptor 4 in mesenchymal stem cells. Stem Cell Res. 2015;1:231–9.
37. Lin YK, Zhu P, Wang WS, Sun K. Serum amyloid A, a host-derived DAMP in pregnancy? Front Immunol. 2022;13:978929.

Povezanost između sistemske inflamacije i metabolizma lipida u razvoju preeklampsije

Tamara Gojković[1*], Daniela Ardalić[2], Gorica Banjac[2], Jelena Vekić[1], Aleksandra Zeljković[1], Jelena Munjas[1], Milica Miljković-Trailović[1], Snežana Jovičić[1], Marija Sarić Matutinović[1], Vesna Spasojević-Kalimanovska[1], Željko Miković[2,3] i Aleksandra Stefanović[1]

[1]Katedra za medicinsku biohemiju, Farmaceutski fakultet Univerziteta u Beogradu, Srbija

[2]Ginekološko-akušerska klinika Narodni front, Beograd, Srbija

[3]Ginekološko-akušersko odeljenje, Medicinski fakultet Univerziteta u Beogradu, Srbija

* Autor za korespondenciju: Tamara Gojković, e-mail: tgojkovic@pharmaci.bg.ac.rs

Kratak sadržaj

Preeklampsija (PE) je komplikacija trudnoće koju karakterišu hipertenzija (≥ 140/90 mmHg) i proteinurija (≥ 300 mg/24 h), sa nejasnom patogenezom koja uključuje inflamaciju i dislipidemiju. Cilj ove studije bio je longitudinalno ispitivanje promena u koncentracijama parametara lipidnog statusa i inflamatornim markerima kod trudnica sa visokim rizikom za razvoj PE i onih koje su razvile PE. Od 91 žene, 20 je razvilo PE (PE grupa), a 71 je bila visokorizična (HR grupa). Obe grupe su praćene u četiri vremenske tačke: T1-prvi, T2-drugi, T3-treći trimestar, i T4-predporođaj. Kvantifikovani su lipidni parametri (trigliceridi (TG), ukupni holesterol (TC), HDL-C, LDL-C, apolipoproteini A-I i B-100) i inflamatorni markeri (visokoosetljivi C-reaktivni protein (hsCRP), rezistin, serumski amiloid A (SAA) i monocitni hemoatraktantni protein-1 (MCP-1)). Rezultati su pokazali značajno veće koncentracije TG, resistina i MCP-1 u PE grupi u odnosu na HR grupu u T1 ($p < 0.05$, $p < 0.01$, $p < 0.01$, respektivno). Tokom trudnoće, obe grupe su pokazale porast koncentracija TC, LDL-C, TG, SAA i MCP-1 ($p < 0.001$), dok su koncentracije HDL-C i resistina značajno porasle samo u HR grupi ($p < 0.001$). Razvoj PE je povezan sa aterogenim promenama lipidnog statusa, okarakterisanim hipertrigliceridemijom, bez promena u HDL-C koncentracijama, pri čemu povećanje SAA potencijalno smanjuje zaštitnu ulogu HDL-a.

Ključne reči: preeklampsija, visokorizična trudnoća, lipidni profil, inflamacija