folia medica

Folia Medica 63(4):511-8
DOI: 10.3897/folmed.63.e56489

Original Article

High-Sensitivity CRP Levels In Women with Gestational Hypertension, Preeclampsia and in Normotensive Pregnant Women and Its Correlations

Dolina G. Gencheva[1,2], Fedya P. Nikolov[1,2], Ekaterina H. Uchikova[3,4], Rosen D. Mihaylov[5,6], Blagovesta G. Pencheva[5], Katerina I. Ivanova[3,4]

[1] *Cardiology Section, First Department of Internal Diseases, Medical University of Plovdiv, Plovdiv, Bulgaria*
[2] *Clinic of Cardiology, St George University Hospital, Plovdiv, Bulgaria*
[3] *Department of Obstetrics and Gynaecology, Medical University of Plovdiv, Plovdiv, Bulgaria*
[4] *Clinic of Obstetrics and Gynaecology, St George University Hospital, Plovdiv, Bulgaria*
[5] *RAMUS Independent Medical Diagnostic Laboratory, Sofia, Bulgaria*
[6] *Jordanka Filaretova Medical College, Sofia, Bulgaria*

Corresponding author: Dolina G. Gencheva, Cardiology Section, First Department of Internal Diseases, Medical University of Plovdiv, 66 Peshtersko shose Blvd., Plovdiv, Bulgaria; E-mail: sylvanas@mail.bg; Tel.: +359 878 239 097

Received: 15 July 2020 ♦ **Accepted:** 24 Sep 2020 ♦ **Published:** 31 Aug 2021

Citation: Gencheva DG, Nikolov FP, Uchikova EH, Mihaylov RD, Pencheva BG, Ivanova KI. High-sensitivity CRP levels in women with gestational hypertension, preeclampsia and in normotensive pregnant women and its correlations. Folia Med (Plovdiv) 2021;63(4):511-8. doi: 10.3897/folmed.63.e56489.

Abstract

Introduction: Gestational hypertension is a less investigated hypertensive disorder of pregnancy than preeclampsia, but evidence exists of an unfavourable cardiovascular profile for women after such a pregnancy.

Aim: To determine serum high-sensitivity C-reactive protein (hs-CRP) levels in women with preeclampsia, gestational hypertension, and in normotensive pregnancy in order to assess the cardiovascular implications and to examine its correlations with some characteristics of women.

Materials and methods: Thirty-six women with gestational hypertension, thirty-seven with preeclampsia, and fifty maternal and gestational age-matched controls were included in a single-center prospective clinical-epidemiological study. Serum hs-CRP levels were determined using ELISA method.

Results: Significantly higher hs-CRP levels were found in the gestational hypertension group than in the controls (p=0.043), but not in the preeclampsia group (p=0.445). The levels between the two pathological groups did not differ significantly (p=0.247). Odds ratio for hs-CRP levels higher than the provided cut-off was 3.31 (95% CI 1.32–8.29) for the presence of gestational hypertension. In the normotensive pregnant women, the hs-CRP levels had a positive correlation with BSA, pre-pregnancy and current BMI, but such correlations were absent in the hypertensive groups. There were no correlations with the maternal or gestational age, current weight gain in any of the groups or with the highest detected blood pressure in the pathological groups. These levels did not differ according to gravidity, smoking status and smoking during pregnancy.

Conclusions: Elevation of hs-CRP was more pronounced in women with gestational hypertension than in women with preeclampsia, which could indicate a different pathophysiological mechanism and a higher cardiovascular risk for those women.

Keywords

biomarkers, cardiovascular risk, inflammation, pregnancy, women's health

INTRODUCTION

High-sensitivity CRP is one of the most studied markers of inflammation. It was first discovered in 1930 and initially was thought to be a substance secreted by pneumococcal bacteria during the course of pneumonia.[1] It was found later that it was a protein produced by the liver during the acute phase of infectious, inflammatory, and malignant processes as a non-specific response to tissue damage. It elevates rapidly after a pathological stimulus and has a relatively constant half-life as a result of which its circulating levels depend mainly on the synthesis rate.[2] As early as the 1950s, reports started to emerge of elevated levels of CRP during myocardial infarction[3] and in the 1990s and the following years, its higher levels, including those within the reference range, were found to be associated with a risk of cardiovascular and cerebrovascular events.[4,5] Research in the field was amplified by the emergence of high-sensitivity assays.[6] A study by Wang et al. encompassing over 53 000 people demonstrated that cumulative exposure to higher levels was a dose-dependent risk factor for the aforementioned diseases.[7] Explanation was sought in the theory of atherosclerosis as an inflammatory process and the role of constant low-grade inflammation as an atherogenic factor.[8]

In a statement from 2003, the American Heart Association and the Centres for Disease Control and Prevention designated hs-CRP as a reliable and readily available marker for risk stratification and established relative risk categories according to its levels (Class of recommendation IIa, Level of Evidence B).[9] The European Society of Cardiology acknowledged in the current 2016 prevention guideline that the relative risk associated with hs-CRP levels is similar to the one associated with the classic cardiovascular risk factors, but did not advocate its use in risk stratification, as they doubted its added value to the endorsed SCORE system. However, they do not deny its use in specific scenarios and populations.[10]

Hypertensive complications of pregnancy on the other hand emerged in the past decades as a risk factor for future cardiovascular events in women and are viewed by some authors as a failed cardiovascular "stress test" of the female organism that is a very early prodrome of unfavourable outcomes.[11,12] In large cohort studies of women years after the target hypertensive pregnancy, there was a higher risk for arterial hypertension, type 2 diabetes mellitus, venous thromboembolism, dyslipidemia, coronary artery disease, stroke, heart failure, and cardiovascular mortality.[13-17] Usually, the risk is proportionate to the severity of the disease and is reported to be more pronounced in preeclampsia than in gestational hypertension where investigations of both forms are available.

Although hypertensive complications of pregnancy are quite common and are associated with a high maternal and fetal mortality, their pathological mechanisms are still not completely understood.[18] One of the culprit mechanisms is thought to be an underlying exaggerated inflammatory response of the maternal organism as a result of the improper placentation and the following placental ischemia.[19,20] Gestational hypertension is the less investigated of the two forms and is generally considered more benign, but it can progress to preeclampsia and eclampsia as well as lead to serious maternal and fetal complications in severe cases.[21]

Based on the presented literature review, we suspect that a link between low-grade inflammation, as indicated by the hs-CRP levels, hypertensive disorders of pregnancy, and subsequent cardiovascular risk in women exists and aimed to investigate this problem in the present study.

AIM

To determine and compare high-sensitivity CRP levels in women with gestational hypertension, preeclampsia, and in normotensive pregnant women, establish correlations with characteristics of the women and investigate discriminative abilities of hs-CRP and odds ratio (OR) for the presence of the pathologies.

MATERIALS AND METHODS

A single-center prospective clinical-epidemiological study was performed at the Clinic of Cardiology at St George University Hospital in Plovdiv, Bulgaria between August 2018 and January 2020 and data for 123 pregnant women were analyzed. Thirty-seven of those women had preeclampsia, 36 had gestational hypertension, and 50 were normotensive pregnant controls. One-hundred and sixteen of the women had singleton pregnancies and nine had bigeminal pregnancies (4 in the preeclampsia group, 2 in gestational hypertension and 3 in tne controls). The women were enrolled from the Clinic of Obstetrics and Gynecology at the same hospital and some of the controls were referred by local Obstetrics and Gynecology practices. The study was approved by the Ethics Committee of the Medical University of Plovdiv and all of the participants signed a written informed consent before participation. Current weight and height of the women were measured with standardized equipment at the Clinic of Obstetrics and Gynecology. Weight before the pregnancy was self-reported. Based on those values, body mass index (BMI) and body surface area (BSA; using DuBois & DuBois formula) were calculated. Women were diagnosed with preeclampsia if high blood pressure (office measured systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg at least twice over the course of minimum 4 hours apart) was registered for the first time after gestational week 20 and also had proteinuria of ≥300 mg for 24 hours in at least one measurement. The women with gestational hypertension covered the same criteria for blood pressure, but registered proteinuria had to be less than 300 mg for 24 hours.[22]

The participants were classified further as having early forms of the conditions if the hypertension was first regis-

tered before gestational week 34 and having severe forms if the highest reported values of blood pressure were systolic blood pressure (SBP) ≥160 mmHg and/or diastolic blood pressure (DBP) ≥110 mmHg. One woman from the preeclampsia group was additionally classified as having a severe form based on levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) twice over the upper reference limit; and one woman from the gestational hypertension group had ALT twice over the upper reference limit, but was already classified as severe due to blood pressure values.[22] We did not include women who at the time of the enrolment had pulmonary edema, encephalopathy, epigastric pain or the constellation of HELLP syndrome as such conditions were considered a medical emergency or any other women whose participation in the study could possibly delay obstetric or other necessary interventions. Individuals under the age of 18, those with history of chronic hypertension, diabetes mellitus or any other serious systemic conditions, cardiovascular diseases, recent inflammatory diseases, trauma and active malignancies were excluded from the study. Specifically for the control group, no women with diagnosed intrauterine growth restriction were included.

High sensitivity C-reactive protein was determined using Sandwich ELISA (DIAsource ImmunoAssays S.A., Louvain-la-Neuve, Belgium) with an anti-CRP monoclonal antibody. A six-point calibration curve was built (0 ng/ml; 100 ng/ml; 400 ng/ml; 1000 ng/ml; 4000 ng/ml; 10,000 ng/ml). The lower detection limit was 10 ng/ml. Serum was separated from venous blood after centrifuging at 3000 RPM for 10 minutes and was then stored at –20°C as per manufacturer's instructions until the test was performed following the manufacturer's protocol.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics 25.0 (IBM SPSS Statistics for Windows, SPSS Inc., Chicago, IL, USA) and MedCalc Version 14.8.1 (MedCalc Software, Mariakerke, Belgium). Continuous variables were tested for normality with Kolmogorov-Smirnov and Shapiro-Wilk tests. The Student's t-test, analysis of variance (ANOVA) test, and Bonferroni post hoc test were used to compare the continuous variables that had normal distribution more than two independent groups with homogeneity of variances. The continuous variables with non-normal distribution were compared with the Kruskal-Wallis test and the Mann-Whitney U test. The relationship between categorical variables in cross tables was analyzed using the χ^2 test and Fisher's exact test. Correlations analysis was performed using either Pearson's correlation coefficient or Spearman's *rho* according to the normality of the continuous variables. Receiver Operating Characteristics (ROC) curve analysis was carried out to determine discriminative abilities of hs-CRP. The optimal cut-off value was obtained from the Youden index [maximum (sensitivity + specificity–1)]. Logistic regression was performed to explain the relationship between variables. Findings with $p<0.05$ were considered statistically significant.

RESULTS

Study population

The women in the study groups were maternal and gestational age matched and there was no statistical difference between the percentage of non-smokers and smokers and women smoking during the current pregnancy in the groups. The two pathological groups did not differ significantly for the presence of early and severe forms. BSA, pre-pregnancy and current BMI were significantly higher in the hypertensive women compared to controls, but there was no statistically significant difference in current weight gain between the groups. More primigravid women were in the gestational hypertension group than in the groups of the controls and fewer were pregnant with their second pregnancy in the gestational hypertension group than in the controls **(Table 1)**.

High sensitivity CRP

Mean serum levels of hs-CRP were higher in the gestational hypertension group, compared to the controls (6441.12±3124.17 ng/ml vs. 5095.61±3086.67 ng/ml, $p=0.043$), but there was no significant difference between the mean levels in the preeclampsia group and the controls, despite a tendency for higher levels in preeclampsia (5581.02±3036.28 ng/ml vs. 5095.61±3086.67 ng/ml, $p=0.445$). The mean levels between the gestational hypertension group and the preeclampsia group did not differ significantly (6441.12±3124.17 ng/ml vs. 5581.02±3036.28 ng/ml, $p=0.247$). There was borderline significant difference when comparing only the severe forms of gestational hypertension and preeclampsia together to the controls (6453.04±2916.13 ng/ml vs. 5095.61±3086.67 ng/ml, $p=0.063$).

There was no significant difference between the hs-CRP levels in the women when divided into subgroups according to gravidity, smoking status and smoking during pregnancy **(Table 2)**. Correlation analysis **(Table 3)** was conducted and a significant correlation between hs-CRP levels and certain characteristics of the women was found. In the whole study group, hs-CRP correlated positively with BMI before pregnancy, current BMI, and BSA of the women, but when analyzed separately into groups, these correlations were present only for the group of the controls and not in the gestational hypertension and the preeclampsia groups. There was no correlation between hs-CRP levels and maternal age, gestational age, weight gain and for the pathological groups with the maximum reported SBP or DBP.

ROC curve analysis was performed in order to assess the ability of hs-CRP to differentiate between the controls and the gestational hypertension group and it gave an area under the curve of 0.63, $p=0.043$ for levels higher than the

Folia Medica

Table 1. Characteristics of the study population

Groups	Controls			Gestational hypertension			Pre-eclampsia		
	n	$\bar{X}$	SD	n	$\bar{X}$	SD	n	$\bar{X}$	SD
Maternal age (years)	50	30.82[a]	6.02	36	28.83[a]	5.78	37	29.81[a]	5.14
Gestational age (weeks)	50	34.08[a]	5.23	36	33.71[a]	4.08	37	33.24[a]	3.74
BMI before pregnancy (kg/m^2)	49	22.58[a]	5.11	35	28.58[b]	6.14	35	27.26[b]	5.68
BMI – current (kg/m^2)	50	27.81[a]	5.49	36	33.66[b]	5.75	36	31.77[b]	5.32
Weight gain (kg)	49	14.05[a]	6.18	35	13.69[a]	6.54	36	12.94[a]	7.51
BSA (m^2)	50	1.83[a]	0.20	36	1.97[b]	0.20	37	1.96[b]	0.18
	n	%	Sp	n	%	Sp	n	%	Sp
Smoking									
Non smoker	13	26.0[a]	6.2	15	41.7[a]	8.2	15	40.5[a]	8.1
Former smoker	10	20.0[a]	5.7	2	5.6[a]	3.8	3	8.1[a]	4.5
Smoker	27	54.0[a]	7.0	16	44.4[a]	8.3	17	45.9[a]	8.2
Smoking during pregnancy	14	51.9[a]	9.6	6	37.5[a]	12.1	8	47.1[a]	12.1
Gravidity									
1	12	24.0[a]	6.0	20	55.6[bc]	8.3	16	43.2[ac]	8.1
2	22	44.0[a]	7.0	7	19.4[bc]	6.6	12	32.4[ac]	7.7
3+	16	32.0[a]	6.6	9	25.0[a]	7.2	9	24.3[a]	7.1
Early forms	-	-	-	26	72.2	7.5	31	83.8	6.1
Severe forms	-	-	-	13	36.1	8.0	13	35.1	7.8

One lowercase letter indicates lack of statistical difference, while different lowercase letters indicate presence of statistical difference (p<0.05)

Table 2. Comparative analysis of hs-CRP levels and gravidity, smoking status of the women and smoking during pregnancy by groups

	Gravidity								
	1			2			3+		
	n	$\bar{X}$	SD	n	$\bar{X}$	SD	n	$\bar{X}$	SD
Whole sample	48	5640.71[a]	3021.98	41	5451.52[a]	3112.78	34	5849.77[a]	3296.70
Controls	12	5547.21[a]	3193.28	22	4414.88[a]	2875.65	16	5692.92[a]	3293.18
GH	20	6153.05[a]	3150.62	7	7518.29[a]	2403.58	9	6243.47[a]	3677.95
PE	16	5070.41[a]	2803.50	12	6146.41[a]	3301.79	9	5734.93[a]	3275.85
GH + PE	36	5671.88[a]	3009.10	19	6651.84[a]	3008.36	18	5989.20[a]	3388.84
	Smoking status								
	Never			Former			Current		
Whole sample	43	5904.23[a]	2899.22	15	4195.53[a]	3003.23	60	5632.58[a]	3282.58
Controls	13	4647.84[a]	2886.81	10	4356.10[a]	3494.19	27	5585.10[a]	3053.48
GH	15	6697.87[a]	2865.14	2	3743.50	3174.20	16	6356.01[a]	3631.52
PE	15	6199.47[a]	2762.30	3	3961.67	1655.45	17	5027.11[a]	3361.94
GH + PE	30	6448.67[a]	2776.83	5	3874.40	1975.71	33	5671.42[a]	3505.43
	Smoking during pregnancy						p		
	No			Yes					
Whole sample	32	5855.11	3554.49	28	5378.26	2985.66	0.477		
Controls	13	5525.05	3587.92	14	5640.86	2599.53	0.924		
GH	10	7338.62	3573.85	6	4718.33	3379.95	-		
PE	9	4683.51	3287.44	8	5413.65	3627.80	0.669		
GH + PE	19	6080.94	3611.73	14	5115.66	3407.06	0.397		

GH: gestational hypertension; PE: preeclampsia; One lowercase letter indicates lack of statistical difference (p<0.05). Subgroups with n<8 were not analyzed due to lack of statistical representability.

Table 3. Correlation coefficients between hs-CRP levels and certain characteristics of the women

Characteristics	All women	Controls	Gestational hypertension	Preeclampsia
Maternal age	−0.043	0.035	−0.006	−0.081
Gestational age	0.104	0.176	0.264	−0.112
BMI before pregnancy	0.270**	0.360*	0.273	0.068
Current BMI	0.325***	0.442**	0.326	0.096
BSA	0.280**	0.414**	0.164	0.121
Current weight gain	0.122	0.125	0.118	0.142
Maximum SBP	-	-	0.089	0.187
Maximum DBP	-	-	0.181	0.107

* $p<0.05$; ** $p<0.01$; *** $p<0.001$

selected cut-off value of 5446 ng/ml with sensitivity of 72%, specificity of 56%, positive predictive value of 54%, and negative predictive value of 74% **(Fig. 1)**. It could not differentiate between the controls and the preeclampsia group (AUC - 0.548, p=0.445) (**Fig. 2**).

Binary logistic regression was performed in order to quantify the role of hs-CRP as an indicator for gestational hypertension and the odds ratio (OR) was 3.31 (95% CI 1.32–8.29) for the presence of gestational hypertension in women with values higher than the cut-off of 5446 ng/ml.

DISCUSSION

Women in our pathological groups were statistically equivalent when it comes to severity and onset of the disease. Moreover, the criteria used for severity were the same in the gestational hypertension and the preeclampsia groups. All of the severe forms in gestational hypertension group were classified as such according to blood pressure values and one woman had both the blood pressure criterion and elevated ALT levels twice over the upper limit. In the preeclampsia group, all women with severe forms were according to blood pressure values and one woman was further classified in this groups due to having both AST and ALT significantly elevated. Truly severe forms of preeclampsia (such as HELLP syndrome, pulmonary edema and encephalopathy) were omitted for reasons given in the Materials and methods section. The hypertensive women as a result had homogenous characteristics as far as severity and onset were concerned and the only discriminator was the presence or lack of proteinuria of more than 300 mg for 24 hours. In this setting, the hs-CRP levels were statistically the same between the two pathologies, but only the gesta-

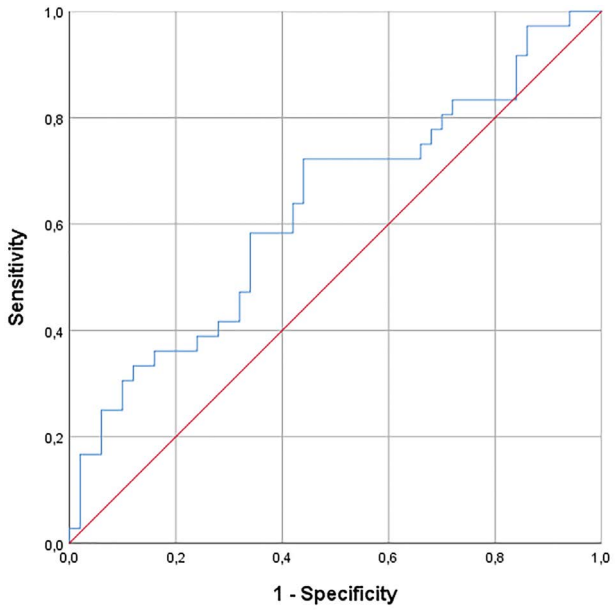

Figure 1. ROC curve for hs-CRP for differentiating between the controls and the gestational hypertension group with area under the curve 0.63, p=0.043.

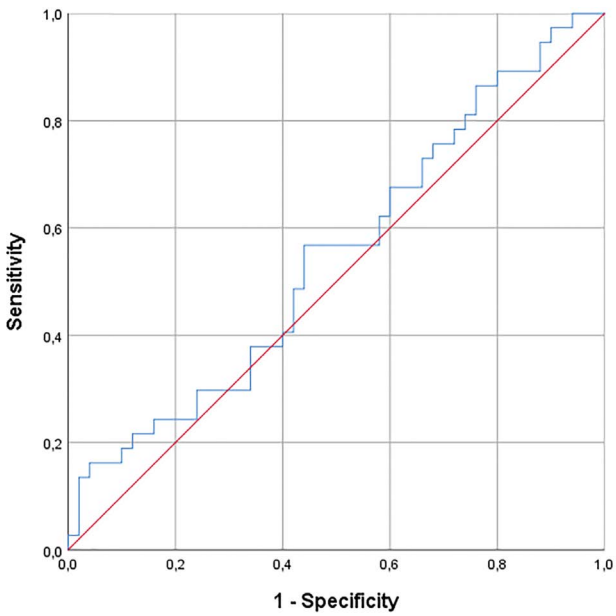

Figure 2. ROC curve for hs-CRP for differentiating between the controls and the preeclampsia group with area under the curve 0.548, p=0.445.

Folia Medica

tional hypertension group reached statistically significant difference from the controls, while there was only a tendency for higher values in the preeclampsia group. These results imply a more marked inflammatory response in the women with pregnancy-induced hypertension without proteinuria and could support the hypothesis of the dominance of different etiological and pathophysiological mechanisms in the two hypertensive disorders, although they are often viewed as forms of the same disease.[23]

In a study by Jannesari et al.[24], the authors did not find significantly different levels of serum hs-CRP between women with mild preeclampsia and controls and such difference was present only when comparing the severe forms to the controls. In another study by Fink et al.[25] the presence of preeclampsia was not associated with higher hs-CRP levels. The explanations for the lack of significantly elevated hs-CRP in our preeclampsia group could be the prevalence of mild forms in it (64.9%). The small percentage of severe forms in our study group (36.1% in gestational hypertension and 35.1% in preeclampsia) reflects in fact the prevalence of those forms in a 1980-2010 cohort study conducted in the USA analyzing 120 million women who gave birth during this time period, in which the severe forms were 1.4% out of 3.8% (~ 36.8%) women with preeclampsia in 2010.[26]

There are fewer studies investigating gestational hypertension than studies investigating preeclampsia, yet we managed to identify a recent study by Rout et al. who also found elevated levels of hsCRP in the second and third trimester of women with gestational hypertension.[27]

ROC curve analysis in our study for the differentiation between gestational hypertension and normotensive pregnancies is with a slightly larger AUC of 0.63 (sensitivity 72% and specificity 56%), than the results of Jannesari et al.[24], who reported an AUC of 0.61 for discriminating between preeclampsia and the controls with a sensitivity of 62.7% and specificity of 56%; but still AUC in the current study did not reach the threshold for satisfactory discriminating abilities of 0.7. Nonetheless, levels of hs-CRP higher than the estimated cut-off of 5446 ng/ml in our study were associated with a 3.31 higher chance for the presence of gestational hypertension compared to women below the cut-off value.

In our study, significant correlations between hs-CRP and the characteristics of the women existed only for the normotensive women, which could indicate that in the hypertensive groups, the levels were mostly determined by the presence of the pathology. Similarly to our findings, in other studies, hs-CRP levels were reported to be positively correlated with higher BMI in non-pregnant populations.[28,29] Lack of significant change of hs-CRP for the duration of pregnancy was established by Watts et al. when sampling the same healthy gravid women twice after mid-pregnancy, which possibly is consistent with our findings of no correlation between hs-CRP levels and gestational age in any of the groups.[30] Hs-CRP levels, which are known to be elevated with age, did not correlate with maternal age in our study population, which could be due to the fact that its levels are reported to be higher in populations older than 45 years, which are not represented in our study.[31]

Finally, evidence of higher hs-CRP levels in gestational hypertension, but not in preeclampsia in our study, could be in line with several large studies which confirmed a higher risk in women after gestational hypertension when compared to women who had preeclampsia for the development of a vast number of diseases, known to be associated with low-grade inflammation: arterial hypertension[32], type 2 diabetes mellitus, hypercholesterolemia[33], ischemic heart disease, myocardial infarction, death from myocardial infarction, heart failure, and chronic kidney disease[34]. This theory seems plausible as Brown et al. discovered elevated levels of hs-CRP in women years after a hypertensive pregnancy, even after adjustment for BMI and other cardiovascular risk factors.[35]

Limitations of the study

Relatively small sample size.

CONCLUSIONS

Hs-CRP levels were higher in gestational hypertension, but not in preeclampsia when compared to controls, possibly due to the presence of different underlying pathophysiological mechanisms in the two conditions. Discriminative abilities of hs-CRP for the presence of gestational hypertension are not satisfactory and therefore we do not advise its use as a screening test. Nonetheless, women with levels higher than the provided cut-off were 3.31 times more likely to have gestational hypertension. There was no correlation in either of the pathological groups with characteristics of the women. Since low-grade inflammation is now believed to be involved in the development of a large number of cardiovascular diseases, attention should be drawn to all women with hypertensive disorders of pregnancy, as the lack of proteinuria does not seem to indicate a more benign risk profile. In normotensive pregnant women on the other hand, hs-CRP levels correlated significantly and positively with BMI and BSA.

Funding

The study was financially supported for the purchase of the biomarker kits by a scientific project of the Medical University of Plovdiv, "DPDP N19/2019" via the "Doctoral and postdoctoral projects" program.

Conflict of Interest

The authors declare that no competing interests exist.

Acknowledgements

The authors would like to express their gratitude to the women who participated in the study and to the personnel of the Clinic of Obstetrics and Gynecology at St George University Hospital in Plovdiv.

REFERENCES

1. Ansar W, Ghosh S. CRP: historical perspective, structure, evolution, synthesis, clinical and biological functions. In: Ansar W, editor. Biology of C Reactive Protein in Health and Disease. New Delhi: Springer: 2016:33–43.
2. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest 2003; 111(12):1805–12.
3. Kroop I, Shackman N. Levels of C-reactive protein as a measure of acute myocardial infarction. Proc Soc Exp Biol Med 1954; 86:95–7.
4. Ridker PM, Cushman M, Stampfer MJ, et al. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. NEJM 1997; 336(14):973–9.
5. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol 2018; 9:754.
6. Fu Y, Wu Y, Liu E. C-reactive protein and cardiovascular disease: From animal studies to the clinic (Review). Exp Ther Med 2020; 20(2):1211–9.
7. Wang A, Liu J, Li C, et al. Cumulative exposure to high-sensitivity C-reactive protein predicts the risk of cardiovascular disease. J Am Heart Assoc. 2017; 6(10):e005610.
8. Eltoft A, Arntzen KA, Hansen JB, et al. C-reactive protein in atherosclerosis - a risk marker but not a causal factor? A 13-year population-based longitudinal study: The Tromsø study. Atherosclerosis 2017; 263:293–300.
9. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centres for Disease Control and Prevention and the American Heart Association. Circulation 2003; 107(3):499–511.
10. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016; 37(29):2315–81.
11. Craici I, Wagner S, Garovic VD. Preeclampsia and future cardiovascular risk: formal risk factor or failed stress test? Ther Adv Cardiovasc Dis 2008; 2(4):249–59.
12. Banerjee M, Cruickshank JK. Pregnancy as the prodrome to vascular dysfunction and cardiovascular risk. Nat Clin Pract Cardiovasc Med 2006; 3:596–603.
13. Lykke JA, Langhoff-Roos J, Sibai BM, et al. Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother. Hypertension 2009; 53(6):944–51.
14. Marin RM, Portal CG, Sánchez M, et al. Long-term prognosis of hypertension in pregnancy. Hypertens Pregnancy 2000; 19:199–209.
15. Leffert LR, Clancy CR, Bateman BT, et al. Hypertensive disorders and pregnancy-related stroke: frequency, trends, risk factors, and outcomes. Obstet Gynecol 2015; 125(1):124–31.
16. Huang CC, Huang CC, Lin SY, et al. Association between hypertensive pregnancy disorders and future risk of stroke in Taiwan: a Nationwide population-based retrospective case-control study. BMC Pregnancy and Childbirth 2020; 20:217.
17. Wu P, Haththotuwa R, Kwok CS, et al. Preeclampsia and future cardiovascular health: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2017; 10(2):e003497.
18. Alkema L, Chou D, Hogan D, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet 2016; 387(10017):462–74.
19. Roberts JM, Hubel CA. The two stage model of preeclampsia: variations on the theme. Placenta 2009; 30 Suppl A(Suppl A):S32–S37.
20. Harmon AC, Cornelius DC, Amaral LM, et al. The role of inflammation in the pathology of pre-eclampsia. Clin Sci (Lond) 2016; 130(6):409–19.
21. Jin Y, Xu H, Wu M, et al. Correlation of gestational hypertension with abnormal lipid metabolism, insulin resistance and D-dimer and their clinical significance. Exp Ther Med 2019; 17(2):1346–50.
22. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122(5):1122–31.
23. Villar J, Carroli G, Wojdyla D, et al. Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions? Am J Obstet Gynecol 2006; 194(4):921–31.
24. Jannesari R, Kazemi E. Level of high sensitive C-reactive protein and procalcitonin in pregnant women with mild and severe preeclampsia. Adv Biomed Res 2017; 6:140.
25. Fink NR, Chawes B, Bønnelykke K, et al. Levels of systemic low-grade inflammation in pregnant mothers and their offspring are correlated. Sci Rep 2019; 9(1):3043.
26. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. BMJ 2013; 347:f6564.
27. Rout R, Mahalik M. Comparison of C-reactive proteins level in gestational hypertension and in normal pregnancy in 2nd and 3rd trimester and its correlation with maternal and foetal outcome. Int J Reprod Contracept Obstet Gynecol 2019; 8(6):2541–8.
28. Lin CC, Kardia SL, Li CI, et al. The relationship of high sensitivity C-reactive protein to percent body fat mass, body mass index, waist-to-hip ratio, and waist circumference in a Taiwanese population. BMC Public Health 2010; 10:579.
29. Kawamoto R, Kusunoki T, Abe M, et al. An association between body mass index and high-sensitivity C-reactive protein concentrations is influenced by age in community-dwelling persons. Ann Clin Biochem 2013; 50(Pt 5):457–64.
30. Watts DH, Krohn MA, Wener MH, et al. C-reactive protein in normal pregnancy. Obstet Gynecol 1991; 77(2):176–80.
31. Tang Y, Liang P, Chen J, et al. The baseline levels and risk factors for high-sensitive C-reactive protein in Chinese healthy population. Immun Ageing 2018; 15:21.
32. Behrens I, Basit S, Melbye M, et al. Risk of post-pregnancy hypertension in women with a history of hypertensive disorders of pregnancy: nationwide cohort study. BMJ 2017; 358:j3078.
33. Stuart JJ, Tanz LJ, Missmer SA, et al. Hypertensive disorders of pregnancy and maternal cardiovascular disease risk factor development: an observational cohort study. Ann Intern Med 2018; 169(4):224–32.

34. Mannisto T, Mendola P, Vaarasmaki M, et al. Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation 2013; 127(6):681–90.

35. Brown CM, Turner ST, Bailey KR, et al. Hypertension in pregnancy is associated with elevated C-reactive protein levels later in life. J Hypertens 2013; 31(11):2213–9.

Высокочувствительный CRP у женщин с гестационной гипертензией, преэклампсией и при нормотензивной беременности и их корреляции

Долина Г. Генчева[1,2], Федя П. Николов[1,2], Екатерина Х. Учикова[3,4], Росен Д. Михайлов[5,6], Благовеста Г. Пенчева[5], Катерина И. Иванова[3,4]

[1] *Отделение кардиологии, Первая кафедра внутренних болезней, Медицинский университет – Пловдив, Пловдив, Болгария*

[2] *Клиника кардиологии, УМБАЛ „Св. Георги", Пловдив, Болгария*

[3] *Кафедра акушерства и гинекологии, Медицинский университет – Пловдив, Пловдив, Болгария*

[4] *Клиника акушерства и гинекологии, УМБАЛ „Св. Георги", Пловдив, Болгария*

[5] *Независимая медико-диагностическая лаборатория РАМУС, София, Болгария*

[6] *Медицинский колледж „Йорданка Филаретова", София, Болгария*

Адрес для корреспонденции: Долина Г. Генчева, Отделение кардиологии, Первая кафедра внутренних болезней, Медицинский университет – Пловдив, бул. „Пещерско шосе" № 66, Пловдив, Болгария; E-mail: sylvanas@mail.bg; Тел.: +359 878 239 097

Дата получения: 15 июля 2020 ♦ **Дата приемки:** 24 сентября 2020 ♦ **Дата публикации:** 31 августа 2021

Образец цитирования: Gencheva DG, Nikolov FP, Uchikova EH, Mihaylov RD, Pencheva BG, Ivanova KI. High-sensitivity CRP levels in women with gestational hypertension, preeclampsia and in normotensive pregnant women and its correlations. Folia Med (Plovdiv) 2021;63(4):511-8. doi: 10.3897/folmed.63.e56489.

Резюме

Введение: Гестационная гипертензия является менее изученной гипертонической патологией беременности, чем преэклампсия, но есть данные о неблагоприятном сердечно-сосудистом профиле у женщин после такой беременности.

Цель: Определить уровни сывороточного высокочувствительного С-реактивного белка (hs-CRP) у женщин с преэклампсией, гестационной гипертензией и нормальной беременностью, чтобы оценить сердечно-сосудистые эффекты и изучить корреляцию с некоторыми характеристиками женщин.

Материалы и методы: Тридцать шесть женщин с гестационной гипертензией, 37 женщин с преэклампсией и 50 здоровых женщин в качестве контрольной группы равного материнского и гестационного возраста были включены в эндоцентрическое проспективное клинико-эпидемиологическое исследование. Уровни hs-CRP в сыворотке определяли с помощью ELISA.

Результаты: Значительно более высокие уровни hs-CRP были обнаружены в группе гестационной гипертензии по сравнению с контрольной группой (p=0.043), но не в группе преэклампсии (p=0.445). Уровни девтепатологических групп достоверно не различались (p=0.247). Отношение вероятности для уровней hs-CRP выше порогового значения было 3.31 (95% ДИ 1.32–8.29) для гестационного диабета. Среди нормотонических беременных уровень hs-CRP положительно коррелировал с площадью поверхности тела (ППТ), текущим ИМТ и ИМТ до беременности, но такие корреляции отсутствовали в группе гипертоников. Не было обнаружено корреляций с материнским и гестационным возрастом, прибавкой в весе в любой группе или с самым высоким измеренным артериальным давлением среди патологий. Эти уровни не различались в отношении беременности, статуса курения и курения во время беременности.

Заключение: Увеличение hs-CRP более выражено у женщин с гестационной гипертензией, чем у женщин с преэклампсией, что может быть индикатором другого патофизиологического механизма и более высокого сердечно-сосудистого риска для этих женщин.

Ключевые слова

биомаркеры, сердечно-сосудистый риск, воспаление, беременность, женское здоровье