

Comparison Between High Sensitive C-Reactive Protein Level in Preeclamptic Women and Normal Pregnancy

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Abstract

Introduction: Preeclampsia is an important complication of pregnancy that affects about 2-8% and is characterized by the presence of placental dysfunction due to systemic inflammation. One of the widely used inflammatory markers is high sensitivity C-Reactive Protein (hs-CRP) which is produced by a hypoperfused placenta in preeclampsia. The purpose of this study was to determine the comparison of hs-CRP levels in preeclampsia and normal pregnancies.

Methods: This study is an observational analytic study with a case-control design which was conducted at the Adam Malik General Hospital and network hospitals from February until the number of samples was met. The study subjects were normal pregnant women and preeclampsia in the third trimester who visited the polyclinic. All study subjects underwent history taking, physical examination, and hs-CRP examination through blood samples from the median cubital vein. After data collection was completed, the data were analyzed using the Mann-Whitney test.

Results: This study was followed by 60 study subjects consisting of normal pregnant women and preeclampsia. Study subjects in the preeclampsia group had a higher mean parity, age, gestational age, body mass index, blood pressure and mean arterial pressure than the group of normal pregnant women and found a positive correlation between these variables and hs-CRP levels. Examination of hs-CRP levels in preeclampsia patients was also higher than in normal pregnant patients and there was a significant difference between the two groups ($p = 0.000$).

Conclusion: There was a significant difference between hs-CRP levels in preeclampsia patients with normal pregnant patients and significantly higher hs-CRP levels were found in the preeclampsia group ($p < 0.05$).

Keywords: Preeclampsia, high sensitive c-reactive protein, inflammation.

INTRODUCTION

Preeclampsia is an important complication of pregnancy that affects approximately 2-8% of all pregnancies and is a major cause of maternal, perinatal morbidity, and mortality.^{1,2,3} The main causes of preeclampsia are bleeding, hypertension in pregnancy, and infection.^{2,3} Preeclampsia is characterized by placental dysfunction, and the maternal response to systemic inflammation with endothelial activation and coagulation. One of the

markers of inflammation is C-Reactive Protein (CRP) which can be used as an indicator of the severity of preeclampsia and can detect very low CRP concentrations.^{4,5,6}

High Sensitivity C-Reactive Protein (hs-CRP) is an example of an inflammatory marker produced by a hypoperfused placenta in preeclampsia. hs-CRP is positively correlated with other markers of severity of preeclampsia and negatively correlated with stillbirth and fetal weight with preeclampsia with aggravating symptoms.⁷ this study aimed to compare hs-CRP levels in preeclampsia and normal pregnancies.

METHODS

This study is an observational analytic study with a case-control design which was conducted at the Adam Malik Central General Hospital and a network hospital from February until the number of samples was met. The study subjects selected by consecutive sampling were normal pregnant women and preeclampsia in the third trimester who visited the polyclinic. Pregnant women who had complications in pregnancy or other obstetric complications were excluded from the study.

All study subjects who have signed the informed consent have a history taken regarding identity, gestational age, and comorbidities. Furthermore, examination of vital signs, weight, height, and height of uterine fundus were done. Based on the history taking and physical examination, the study subjects were divided into 2 groups, the preeclampsia, and the normal pregnant group. The hs-CRP examination was carried out by taking ± 3 cc of blood from the median cubital vein and directly processed in the laboratory for study subjects who were at the Adam Malik Central General Hospital, while for study subjects who were in-network hospitals, blood samples were collected collectively during 24 hours and frozen before being sent to Adam Malik Hospital to avoid biased results.

The blood samples obtained were centrifuged at 3,500 rpm for 10 minutes. After that, the serum was taken and the hs-CRP levels in the Architect 8200 plus tool. The data regarding the sociodemographic of the study subjects were arranged in a frequency distribution table, while the inferential data were analyzed using the independent T-test if it was normally distributed and the Mann Whitney test if it was not normally distributed.

RESULTS

This study was followed by 60 research subjects who were divided into 2 groups, normal pregnant women and preeclampsia by consecutive sampling. The results showed that the study subjects in the preeclampsia group had a higher mean parity and age than the normal pregnant women group (2.13 ± 0.73 vs. 1.8 ± 0.61 ; 27.43 ± 0.81 vs. 27.10). ± 1.12 years) (Table 1). The preeclampsia group also had a higher gestational age and body mass index than the normal pregnant group (36.33 ± 0.92 vs 34.60 ± 0.89 ; 27.13 ± 1.10 vs 24.70 ± 1.01) (Table 1).

Table 1. Characteristic of study subjects

Variable	Preeclampsia		Normal	
	Mean	SD	Mean	SD
Parity	2.13	0.73	1.8	0.61
Age (years)	27.43	0.81	27.10	1.12
Gestational age (weeks)	36.33	0.92	34.60	0.89
Body mass index (kg/m ²)	27.13	1.10	24.70	1.01

Based on blood pressure, it was known that the systolic, diastolic, and Mean Arterial Pressure (MAP) in the preeclampsia group was higher than the group of patients with normal pregnancies (169.00 ± 9.22 vs. 116.00 ± 7.70 ; 98.67 ± 8.19 vs. 72.00 ± 7.61 ; 122.11 ± 5.56 vs. 86.66 ± 6.72) (Table 2).

Table 2. Characteristic of blood pressure and hs-CRP

Variable	Preeclampsia		Normal	
	Mean	SD	Mean	SD
Systolic blood pressure (mmHg)	169.00	9.22	116.0	7.70
Diastolic blood pressure (mmHg)	98.67	8.19	72.0	7.61
Mean Arterial Pressure (mmHg)	122.11	5.56	86.66	6.72
hs-CRP (mg/dL)	6.32	1.75	2.51	1.03

The level of hs-CRP in preeclampsia patients was also higher than in normal pregnant patients and there was a significant difference between the two groups ($p = 0.000$) (Table 3).

Tabel 3. Perbedaan kadar hs-CRP

Variable	Preeclampsia	Normal	p
hs-CRP	6.32 ± 1.75	2.51 ± 1.03	0.000*

* Mann-Whitney

The correlation analysis showed that all sociodemographic variables had a positive correlation with the level of hs-CRP, but only the age of the patient did not correlate significantly ($p = 0.226$) (Table 4).

Table 4. Correlation between study subjects' characteristics with the level of hs-CRP

Variable	Value	
	r	P
Parity	0.37*	0.003**
Age (years)	0.159*	0.226**
Gestational age (weeks)	0.662*	0.000**
Body mass index (kg/m ²)	0.773*	0.000**
Systolic blood pressure (mmHg)	0.780*	0.000**
Diastolic blood pressure (mmHg)	0.790*	0.000**
Mean Arterial Pressure (mmHg)	0.788*	0.000**

*Spearman, **Mann-Whitney

DISCUSSION

This study analyzed 60 pregnant women in the third trimester who were divided into groups of preeclampsia and normal pregnancy. The results showed that the parity, age, gestational age, and body mass index were higher in the preeclampsia group than the normal pregnant group and all these variables had a positive correlation with the level of hs-CRP. Similar results were found in the study of Sharmin et al who reported that women with preeclampsia had an older age than normal pregnant women, but there was no significant relationship between these groups (24.58 ± 4.05 vs. 23.92 ± 3.72).⁸ Chen et al and Radin et al concluded that the parity of normal pregnant women was lower than women with mild and severe preeclampsia (2.3 ± 0.6 ; 2.3 ± 0.7 ; 2.5 ± 0.5) and there is a positive correlation between parity and the number of history of abortions with hs-CRP levels.^{9,10} However, different results were found in the study of Fink et al indicating that the number of pregnancies (parity) was not associated with hs-CRP levels.¹¹ Serum hs-CRP concentrations are significantly increased in the last trimester of pregnancy in preeclampsia women compared with normotensive pregnant women and the control group and play a role in the pathogenesis of preeclampsia.¹²

Based on the body mass index, the results of Anaelech's study, the body mass index in the preeclampsia women group was significantly higher than normal pregnant women (29.47 ± 6.90 vs. 26.14 ± 2.92 , $p = 0.012$).¹³ Radin et al also showed a positive correlation between hs-CRP and body mass index, waist-to-hip ratio, and body fat percentage ($r = 0.56$; 0.3 ; 0.50).¹⁰

The results showed that the systolic and diastolic blood pressure, and MAP of patients with preeclampsia were higher than the normal patients and had a positive significant correlation with hs-CRP levels. The systolic and diastolic blood pressure trends were similar to the study of Kumru et al ($p < 0.001$). There was a strong positive correlation between serum hs-CRP levels and diastolic blood pressure ($r = 0.9$, $p = 0.05$).¹⁴ The study of Bansal et al., also reported that higher MAP was found in the severe preeclampsia

group, followed by mild preeclampsia and normal pregnancy. A positive correlation between hs-CRP and MAP was found in the mild and severe preeclampsia groups ($r=0.262, 0.095, 0.350$).¹⁵

Based on the results of the study by Jannesari and Kazemi, the mean level of hs-CRP was significantly higher in preeclampsia women compared to normal pregnancies (7.71 ± 6.19 vs 5.44 ± 3.94 ng/ml; $p = 0.02$). In women with severe preeclampsia, hs-CRP levels (8.99 ± 7.27) were significantly higher than in women with mild preeclampsia (6.7 ± 5.06 ng/ml) ($p = 0.02$).¹⁶ Aziz's study on the levels of hs-CRP and TNF- α in non-pregnant women, normal pregnant women, and women with preeclampsia showed that the highest levels of hs-CRP were found in the group of women with preeclampsia at 9.51 ± 2.57 mg/L, followed by normal pregnant women (7.05 ± 3.18 mg/L) and non-pregnant women (4.63 ± 2.76 mg/L). Statistical results showed that there was a significant difference in hs-CRP levels in the three groups with $p = 0.0001$. The results of TNF- in that study also had the same results as hs-CRP, where the highest levels were found in the group of pregnant women with preeclampsia.¹²

The study of Chen et al on 180 women divided into women with mild preeclampsia, severe preeclampsia, and normal pregnant women, showed that the highest levels of hs-CRP were found in the group of women with severe preeclampsia (5.4 ± 1.6 mg/l), followed by mild preeclampsia (5.4 ± 1.5 mg/l) and control (2.1 ± 1.2 mg/l) and found a significant difference between hs-CRP levels between the two preeclampsia groups ($p < 0.05$). The results also showed a high predictive value of hs-CRP for hypertension due to pregnancy with a value of 0.848-0.974 which means that hs-CRP can be used as a diagnostic marker for hypertension due to pregnancy.⁹ Study by Sharmin et al showed that the mean hs-CRP level in the preeclampsia group (10.48 ± 6.93 mg/L) was significantly higher than the control group (3.45 ± 1.71 mg/L) with p -value = 0.000. The concentration of hs-CRP in mild preeclampsia increased by 62.9%, while in the group of women with severe preeclampsia it increased up to 80%. Analysis of the validity of the hs-CRP examination showed a sensitivity of 68%, specificity of 98%, and diagnostic accuracy of 88%.⁸

Different results were found in the studies of De Jonge et al and Qiu et al, showing that hs-CRP is not a significant marker of preeclampsia when the body mass index factor is included in the multiple regression model. Overweight pregnant women without the elevation of hs-CRP concentrations had 2.5 times risk of developing preeclampsia, while overweight women with elevated hs-CRP concentrations had a 5.5 times risk of developing preeclampsia. This may be due to adipose cells which are the main source of IL-6 secretion and TNF- α which is the primary stimulus for hepatic CRP production.^{6,17}

Preeclampsia is not only associated with high morbidity and mortality but is also considered as a risk factor for vascular disease for both mother and baby. Endothelial cell activation and damage are believed to play an important role in the pathogenesis of preeclampsia and the underlying changes in hemostasis. Therefore, hs-CRP as a marker of inflammation plays an important role in the development of preeclampsia and is an indicator of atherosclerosis and also a risk factor for hypertension.^{17,18}

CONCLUSION

The group of preeclampsia women had older age, higher parity, BMI, gestational age, systolic and diastolic blood pressure, and MAP than the group of normal pregnant women. A significant difference was found between hs-CRP levels in preeclampsia patients with normal pregnant patients and significantly higher hs-CRP levels were found in the preeclampsia group ($p < 0.05$).

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