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Relationship between C-Reactive Protein Levels and Preeclampsia in Pregnant Women

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ABSTRACT

Introduction: Preeclampsia remains a major contributor to maternal morbidity and mortality worldwide, including in Indonesia. Increasing evidence suggests that inflammation plays an important role in its development. C-reactive protein (CRP), an easily accessible inflammatory marker, has been proposed as a potential indicator for early identification. This study aimed to examine the association between CRP levels and preeclampsia in pregnant women.

Material and Methods: A case–control study was conducted at RSI A. Yani Surabaya between August and October 2022. Fifty pregnant women beyond 20 weeks of gestation were enrolled, consisting of 25 normotensive and 25 preeclamptic participants. CRP levels were measured using the ichromsa™ system following standard laboratory procedures. Data were analyzed using the Mann–Whitney U test with a significance level of $p<0.05$.

Results: The mean maternal age was slightly higher in the preeclampsia group. Most participants were in the late third trimester. CRP levels differed significantly between groups, with higher values observed among women with preeclampsia ($p<0.001$). A greater proportion of preeclamptic women had CRP concentrations ≥5 mg/L.

Conclusion: This study demonstrates a significant difference in CRP levels between normotensive and preeclamptic pregnancies, supporting the role of inflammation in the condition. However, given the limited sample size and lack of adjustment for confounding factors, the findings should be interpreted cautiously. Larger studies with broader analytical approaches are needed before CRP can be considered for clinical screening or risk stratification.

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INTRODUCTION

Preeclampsia is a hypertensive disorder of pregnancy that affects approximately 2–8% of pregnancies worldwide and remains a major contributor to maternal and perinatal morbidity and mortality [1]. The condition is characterized by new-onset hypertension after 20 weeks of gestation, accompanied by proteinuria or signs of organ dysfunction, as defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP) [2]. Although extensive research has been conducted, the precise mechanisms underlying preeclampsia are not fully understood, and its onset remains difficult to predict [3].

In Indonesia and other low- and middle-income countries, preeclampsia continues to account for a substantial proportion of maternal deaths, emphasizing the need for early identification strategies that are both practical and accessible [4,5]. Recent evidence highlights the role of systemic inflammation in the pathogenesis of

preeclampsia, alongside abnormal placentation, oxidative stress, and endothelial dysfunction [6,7]. These interrelated processes contribute to the clinical manifestations and complications observed in affected pregnancies.

C-reactive protein (CRP), an acute-phase inflammatory marker, has been studied as a potential biomarker associated with preeclampsia. CRP is widely available, cost-effective, and routinely used in many clinical settings, making it an attractive candidate for resource-limited environments [8–10]. Similar findings have been emphasized in recent community-based studies in Indonesia, highlighting the practicality of CRP testing as a screening or educational tool in maternal health programs [11]. Several studies have reported significantly higher CRP concentrations in preeclamptic women compared with normotensive controls [8,12,13].

A recent systematic review also concluded that elevated CRP may reflect the heightened inflammatory state in preeclampsia, although the authors emphasized substantial heterogeneity across studies and highlighted the lack of standardized cut-off values [14]. Meta-analyses and larger cohort studies conducted in the past decade further support the association between inflammatory markers and preeclampsia, though predictive accuracy remains inconsistent [15].

Differences in study design, laboratory techniques, population characteristics, and failure to adjust for confounding factors such as BMI and infection have contributed to the variability in findings across research settings. Therefore, while CRP shows potential as an adjunctive marker, additional evidence from diverse populations is needed to determine its clinical utility.

In Indonesia, data exploring CRP in relation to preeclampsia remains limited. This study was conducted to examine the association between CRP levels and preeclampsia among pregnant women in Surabaya. The findings aim to provide preliminary insight into the inflammatory profile of preeclampsia within the local population and to contribute to ongoing efforts to identify accessible biomarkers for use in routine antenatal care.

MATERIAL AND METHODS

This study employed a case–control design to examine the relationship between C-reactive protein (CRP) levels and preeclampsia. The research was conducted at RSI A. Yani Surabaya, Indonesia, from August to October 2022.

Study Population

Fifty pregnant women with gestational age beyond 20 weeks were recruited consecutively. Participants were divided into two groups: 25 women diagnosed with preeclampsia and 25 normotensive pregnant women. The diagnosis of preeclampsia followed the criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP), which includes new-onset hypertension accompanied by proteinuria or other signs of organ dysfunction [2].

Inclusion and Exclusion Criteria

Eligible participants were women with singleton pregnancies over 20 weeks of gestation and without a prior history of chronic hypertension. Exclusion criteria included multiple gestation, chronic kidney disease, autoimmune disorders, diabetes mellitus, or clinical evidence of acute infection. These conditions were excluded because they may independently influence systemic inflammation and alter CRP levels.

Although major confounders were screened through clinical history and examination, variables such as body mass index (BMI), parity, and subclinical or low-grade infections could not be fully controlled. These factors are recognized contributors to baseline CRP variation and should be considered when interpreting the findings.

Data Collection

Demographic data, obstetric history, blood pressure measurements, and gestational age were obtained through structured interviews and medical record review. Five milliliters of venous blood were collected aseptically from each participant for CRP analysis.

Laboratory Procedures

CRP concentrations were measured using the ichromsa™ fluorescence immunoassay system. The method provides quantitative CRP measurements with relatively short processing times. Calibration of the device was performed using standard reagents provided by the manufacturer. Internal quality checks were carried out daily, and duplicate testing was performed on 10% of randomly selected samples to assess reproducibility.

The cut-off value of ≥ 5 mg/L was used to categorize CRP levels. This threshold is commonly applied in clinical practice to distinguish between normal and elevated CRP based on low-grade systemic inflammation and has been used in previous studies of CRP in pregnancy and hypertensive disorders [8,14]. The choice of this cut-off was therefore based on both clinical convention and its use in earlier research exploring inflammatory markers in preeclampsia.

Statistical Analysis

Statistical analyses were conducted using SPSS version 25. Normality of numerical data was assessed

Table 1. Distribution of Maternal Characteristics

Maternal Characteristics	Normotensive (n=25)	Preeclampsia (n=25)
Age (years)		
≤ 25	5 (20 %)	5 (20 %)
26 – 30	13 (52 %)	10 (40 %)
31 – 35	5 (20 %)	7 (28 %)
> 35	2 (8 %)	3 (12 %)
Gestational Age (weeks)		
31 – 34	0	2 (8 %)
35 – 37	2 (8 %)	6 (24 %)
38 – 39	14 (56 %)	11 (44 %)
≥ 40	9 (36 %)	6 (24 %)

Table 2. Comparison of CRP Levels

CRP Level (mg/L)	Normotensive (n=25)	Preeclampsia (n=25)	p-value
< 5	22 (88 %)	8 (32 %)	
≥ 5	3 (12 %)	17 (68 %)	< 0.001

using the Kolmogorov–Smirnov test. Because CRP levels were not normally distributed, group comparisons were performed using the Mann–Whitney U test. Categorical variables were presented as frequencies and percentages. A p-value<0.05 was considered statistically significant.

Ethical Considerations

This study received ethical approval from the Ethics Committee of RSI A. Yani Surabaya. Participation was voluntary, and all procedures were performed in accordance with the Declaration of Helsinki and local institutional regulations.

RESULTS

A total of 50 pregnant women were included in this study, consisting of 25 normotensive and 25 preeclamptic participants. The mean maternal age was slightly higher in the preeclampsia group compared to the control group. Most participants were in the late third trimester (38–39 weeks of gestation).

Maternal characteristics are summarized in Table 1. Advanced maternal age (>35 years) was more frequent in the preeclampsia group compared to the normotensive group. This finding is consistent with epidemiological data indicating maternal age as an established risk factor for preeclampsia.

Gestational age distribution is presented in Table 1, showing that both groups were predominantly in the late third trimester. However, a higher proportion of preeclamptic women delivered earlier (31–37 weeks) compared to normotensive women, suggesting that preeclampsia may contribute to preterm birth and shorter gestational duration. The primary outcome, CRP levels, showed a statistically significant elevation in preeclamptic women compared to normotensive controls ($p < 0.001$). As shown in Table 2, 88% of normotensive women had CRP <5 mg/L, whereas 68% of preeclamptic women had CRP ≥5 mg/L. The highest CRP concentration recorded in the preeclampsia group was 24.20 mg/L.

Additional analysis revealed that women in the preeclampsia group not only had higher CRP levels but also exhibited a wider range of CRP values compared to the normotensive group. This variability suggests heterogeneity in inflammatory responses among preeclamptic women, which may reflect differences in disease severity or underlying comorbidities.

Moreover, when maternal age and gestational age were examined in relation to CRP levels, women of advanced maternal age (>35 years) and those who delivered earlier (<37 weeks) tended to have higher CRP values. While this study was not powered to test interaction effects, these trends point toward a possible

interplay between maternal characteristics and inflammatory status in the development of preeclampsia.

Taken together, the findings highlight CRP as a potential biomarker that not only distinguishes preeclampsia from normotensive pregnancies but may also provide additional information on disease variability. This supports the rationale for considering CRP in clinical risk stratification and underscores the need for larger studies to explore these associations further.

DISCUSSION

This study found that CRP levels were significantly higher in women with preeclampsia compared with normotensive pregnant women. Although the sample size was limited, the results align with previous research indicating that systemic inflammation plays an important role in the development of preeclampsia. Earlier studies have consistently reported an elevation of inflammatory markers, including CRP, in pregnancies complicated by preeclampsia [1,6,16]. The findings from this study, therefore, add to the growing body of evidence from different populations, including those in low- and middle-income settings.

The higher and more variable CRP concentrations observed in the preeclampsia group may reflect differences in individual inflammatory responses. Preeclampsia is considered a heterogeneous condition with multiple contributing mechanisms, including endothelial dysfunction, oxidative stress, and abnormal placentation [6,17]. These processes stimulate the release of pro-inflammatory cytokines, which in turn increase hepatic production of CRP. The variability seen in this study is consistent with reports that CRP may correlate with disease severity, although the present data did not allow stratification of cases by severity.

CRP has been proposed as a potentially useful biomarker because of its accessibility, low cost, and routine use in many clinical settings [8]. A recent systematic review by Hamadeh et al. reported that CRP is frequently elevated in preeclampsia but emphasized that differences in cut-off values, laboratory techniques, and population characteristics limit comparability across studies [14]. These limitations also apply to the current study. While the use of ≥5 mg/L as a cut-off is consistent with previous work and common clinical practice, the lack of universally accepted thresholds remains a challenge for standardization.

An important consideration in interpreting CRP levels is the potential influence of confounding factors. Although women with acute infection or chronic inflammatory conditions were excluded, this study was unable to fully control for maternal BMI, parity, or subclinical infections, all of which may affect baseline CRP levels [18–20]. The absence of adjustment for these factors reduces the ability to determine whether CRP independently predicts preeclampsia. Future studies with larger samples and multivariable analyses are needed to clarify the extent to which CRP contributes independently to risk assessment.

The gestational age pattern observed in this study is also consistent with the clinical course of preeclampsia. A greater proportion of preeclamptic women delivered before 37 weeks, which corresponds with past research showing an increased likelihood of preterm delivery among women with hypertensive disorders [21,22]. Although not directly related to CRP, this finding supports the clinical relevance of identifying inflammation-related changes earlier in pregnancy.

The possibility of integrating CRP into antenatal screening protocols has been explored in several studies, particularly in low-resource settings where advanced angiogenic biomarkers are not widely available [23]. However, CRP alone is unlikely to provide sufficient discrimination between women who will and will not develop preeclampsia. CRP elevations can occur in a wide range of conditions, limiting specificity. At best, CRP may serve as an adjunct to other risk factors or biomarkers rather than a standalone screening tool [24].

Beyond pregnancy outcomes, elevated CRP during preeclampsia has been linked to long-term cardiovascular risk in mothers and potential metabolic and cardiovascular changes in offspring [15,25]. These associations underscore the importance of understanding inflammatory pathways in preeclampsia, not only for short-term obstetric care but also for long-term health surveillance.

Overall, the findings from this study support the association between CRP and preeclampsia, but the results should be interpreted with caution due to methodological limitations, including the small sample size, single-center design, and lack of adjustment for confounding variables. Further multicenter studies with larger populations and standardized laboratory methods are necessary before CRP can be considered for incorporation into predictive models or clinical decision-making.

CONCLUSION

This study found that CRP levels were higher in women with preeclampsia compared with normotensive pregnant women, supporting the evidence that systemic inflammation contributes to the condition. While these findings add preliminary data from an Indonesian population, they should be interpreted with caution. The

small sample size, single-center design, and the inability to account for important confounding factors limit the strength of the conclusions.

CRP may have potential as an adjunctive marker in understanding the inflammatory profile of preeclampsia, but its role in screening or prediction cannot be determined from this study. Larger, well-designed studies that incorporate multivariable analysis and standardized CRP measurement approaches are needed to clarify whether CRP can contribute meaningfully to risk assessment or early identification of preeclampsia.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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