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Associations of CRP and PCT levels with obstetric and neonatal outcomes: a prospective study

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Abstract

Background C-reactive protein (CRP) and procalcitonin (PCT) levels may be elevated under inflammatory conditions. The aim of this study was to determine the cutoff values for CRP and PCT levels during pregnancy and to evaluate the associations of any elevation with obstetric and neonatal outcomes.

Methods This prospective study was conducted from June 2023 to December 2024. The study included 411 singleton pregnant women aged 18–44 years with no apparent clinical infection. Venous blood samples were collected during the visit for routine antenatal care during all three trimesters. Categorical variables were compared between groups via the chi-square test, and Student's t-test was used to compare normally distributed continuous variables. The area under the ROC curve was used to detect sensitivity and specificity and to set a cutoff. Regression analysis was performed to evaluate the effects of age and BMI on obstetric complications. P values < 0.05 were considered statistically significant.

Results The mean CRP and PCT levels in the study group were 10.9 ± 16.7 and 0.17 ± 1.8, respectively. ROC curves were used to analyze the ability of CRP and PCT values during pregnancy to predict obstetric complications. A cutoff value of 6.72 mg/L (sensitivity: 67%; specificity: 60%) and 0.0385 (sensitivity: 60%; specificity: 61%) was revealed. The incidence of composite obstetric complications was significantly greater in patients with elevated CRP levels (32.4% vs. 67.6%) ($p < 0.001$). The incidence of preeclampsia, GHT, neonatal complications and the need for intensive care were significantly greater in patients with CRP levels > 6.72. The incidence of composite obstetric complications was significantly greater in patients with elevated PCT levels (59% vs. 41%) ($p < 0.001$). Patients with elevated PCT levels had a greater frequency of preterm labor or PPROM, neonatal complications, need for intensive care, and RDS.

Conclusions Elevated CRP and PCT are associated with increased rates of obstetric and neonatal complications. CRP and PCT, which are inexpensive and available, may be used for screening to predict obstetric and neonatal complications during patient follow-up.

Trial registration This study was approved by the institutional ethical committee of the Gazi University Faculty of Medicine (Approval No:05.06.2023/479).

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Keywords C-reactive protein, Procalcitonin, Obstetric complications, Neonatal outcomes, Pregnancy

Background

Prenatal care and continuous monitoring during pregnancy are essential for mitigating obstetric and neonatal complications, which are directly associated with maternal and neonatal morbidity and mortality. These complications include preterm birth, stillbirth, intrauterine growth restriction (IUGR), preeclampsia, gestational diabetes mellitus (GDM), and chorioamnionitis [1]. The primary objective of prenatal follow-up is to evaluate the health status of both the pregnant individual and the fetus while systematically monitoring the pregnancy to identify and manage potential risks.

Prenatal care is a critical component of ensuring maternal and fetal well-being throughout pregnancy. The initial visit during the first trimester typically includes a comprehensive array of assessments aimed at identifying potential risks and establishing baseline health data. These follow-up visits play a vital role in detecting potential obstetric complications and ensuring early intervention when necessary. Therefore, the identification and monitoring of specific biomarkers that can guide the prenatal follow-up process is of paramount importance.

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver in response to inflammation, and it is commonly used as a biomarker in various clinical contexts [2]. Although CRP is not specific to infectious processes, it has been widely utilized in the diagnostic workup of conditions such as chorioamnionitis during pregnancy [3]. CRP levels are generally elevated in normal pregnant individuals compared with nonpregnant individuals. The utility of CRP has been investigated in several obstetric scenarios, including its role in diagnosing subclinical infections in cases of premature rupture of membranes (PROM) [4], assessing the risk of preterm birth [5], and evaluating its association with the development of preeclampsia [6, 7].

Procalcitonin (PCT), a 116-amino acid precursor to the hormone calcitonin, has emerged as another important acute-phase biomarker, particularly in the context of bacterial infections [8]. PCT levels rise rapidly within 3 to 6 h following bacterial infection, making PCT a sensitive marker for distinguishing bacterial from nonbacterial infections. Owing to its rapid response, PCT has gained clinical acceptance in obstetrics, particularly in the diagnosis and management of bacterial infections during pregnancy [3]. In a recent study conducted by Torbé et al., maternal serum procalcitonin levels were evaluated as a potential biomarker for the early diagnosis of neonatal infection and histologic chorioamnionitis. The study revealed that with a threshold of 1.9 ng/mL, the sensitivity of maternal procalcitonin levels for diagnosing neonatal infection and histologic chorioamnionitis was 53% and 75%, respectively, whereas the specificity was reported to be 45% for both conditions [9]. The associations of procalcitonin levels with other pregnancy complications, to our knowledge, have not been previously investigated.

The present study investigated the relationships of CRP and procalcitonin levels across trimesters with obstetric and neonatal outcomes. Specifically, this study aimed to assess whether elevated levels of CRP and procalcitonin are predictive of potential obstetric or neonatal complications and whether these biomarkers could be utilized as effective screening tools in prenatal care.

Methods

Study population and design

This prospective study was conducted at the Gazi University Faculty of Medicine Department of Obstetrics and Gynecology (Ankara, Turkey) between June 2023 and December 2024. This study was approved by the institutional ethical committee of the Gazi University Faculty of Medicine (Approval No: 05.06.2023/479).

The study included 411 singleton pregnant women aged 18–44 years with no apparent clinical infection.

The exclusion criteria were [1] multiple pregnancies; [2] patients with maternal diseases (rheumatological, endocrinological, nephrological, neurological, hematological, oncological, etc.); and [3] clinical maternal infection during blood sample collection (chorioamnionitis, upper respiratory tract infection, urinary tract infection, gastroenteritis, etc.). All patients who participated in the study were informed of the study, and informed consent was obtained from all participants.

For this study, CRP and procalcitonin were measured alongside routine laboratory parameters in maternal blood samples collected during antenatal follow-up visits: at the first visit in the first trimester (6–13 weeks), during second trimester screening (14–18 weeks), and between 30 and 36 weeks of gestation in the third trimester.

The patient's last menstrual period and first trimester ultrasound scans were used to determine gestational age. Preterm labor, PPROM, IUGR, preeclampsia, gestational hypertension (GHT), gestational diabetes mellitus, pregnancy loss, hypothyroidism and cholestasis were included in the composite obstetric complications. Respiratory distress syndrome (RDS), neonatal sepsis, necrotizing enterocolitis (NEC) and intraventricular hemorrhage were included in the composite neonatal complications [10].

Pregnancy loss is defined as the termination of pregnancy before 20 weeks of gestation [11]. Preterm labor

is characterized by the delivery of a fetus between 20 weeks and 0 days and between 36 weeks and 6 days of gestation [12]. Preterm premature rupture of membranes (PPROM) refers to the rupture of fetal membranes prior to 37 weeks of gestation [13].

Preeclampsia was defined as a blood pressure increase of more than 140/90 mmHg after 20 weeks of gestation combined with proteinuria, either more than 300 mg per 24 h or 2 + or more by dipstick [14]. In the absence of proteinuria, preeclampsia is diagnosed as hypertension associated with thrombocytopenia (platelet count less than 100.000/microliter), impaired liver function (elevated blood levels of liver transaminases to twice the normal concentration), new-onset renal insufficiency (elevated serum creatinine greater than 1.1 mg/dL or a doubling of serum creatinine), the development of cerebral or visual disturbances, or pulmonary edema [14]. Gestational hypertension is an increase in blood pressure after 20 weeks of gestation in the absence of proteinuria or any systemic findings [14]. GDM was diagnosed between the 24th and 32nd weeks of gestation, according to the criteria of the International Association of Diabetes and Pregnancy Study Group [15].

Neonatal sepsis is a pathological process that occurs in infants within the first four weeks of life and is characterized by hemodynamic and respiratory alterations resulting from a systemic inflammatory response to an infectious process [16]. Neonatal respiratory distress syndrome is a pulmonary condition that leads to respiratory difficulties in newborns shortly after birth [17]. Therefore, a composite definition of adverse neonatal outcomes was employed, encompassing the presence of one or more of the following criteria: Apgar score < 5 at 5 min, ventilator support within the first 24 h of life (excluding CPAP), cardiopulmonary resuscitation, hypoxic-ischemic encephalopathy, seizure, sepsis, bronchopulmonary dysplasia, persistent pulmonary hypertension, necrotizing enterocolitis (stage II or III), grade III/IV intraventricular hemorrhage, fracture, neonatal brachial plexus palsy, or perinatal death [18].

CRP and procalcitonin measurement

Venous blood samples were collected during the antenatal visit for routine antenatal care during all three trimesters. CRP and procalcitonin measurements were carried out on the same day that blood was taken. The serum CRP levels were evaluated via nephelometric methods on a Siemens brand BN 2 (Siemens Healthineers Corp. Erlangen, Germany) autoanalyzer, and the serum procalcitonin levels were evaluated via electrochemiluminescence methods on a Roche brand Cobas e 601 (Roche Diagnostics GmbH, Hoffmann-La Roche Ltd, Mannheim, Germany) hormone autoanalyzer.

Statistical analysis

SPSS 25.0 statistical software (IBM SPSS Inc., Chicago, IL) was used for data analysis. A priori power analysis was conducted using the G*Power software (version 3.1.9.6) to estimate the required sample size for the overall repeated measures design. Rather than performing separate calculations for each trimester-specific comparison, the power analysis was based on the full longitudinal structure of the study. Drawing on previous studies, a small effect size ($f = 0.1$) was anticipated for CRP and procalcitonin measurements obtained at three gestational time points in patients with and without obstetric or neonatal complications. The alpha level was set at 0.05 and statistical power ($1 - \beta$) at 0.95. It was assumed that the correlation between repeated measurements would be high, and that variances across time points would be unequal. Based on these parameters, the minimum required sample size to achieve adequate statistical power was determined to be 322 participants. Categorical variables were compared between groups via the chi-square test. Student's t test was used to compare normally distributed continuous variables. The area under the receiver operating characteristic (ROC) curve was used to detect sensitivity, specificity, and cutoff. Regression analysis was performed to evaluate the effects of age and body mass index (BMI) on obstetric complications. *P* values < 0.05 were considered statistically significant.

Results

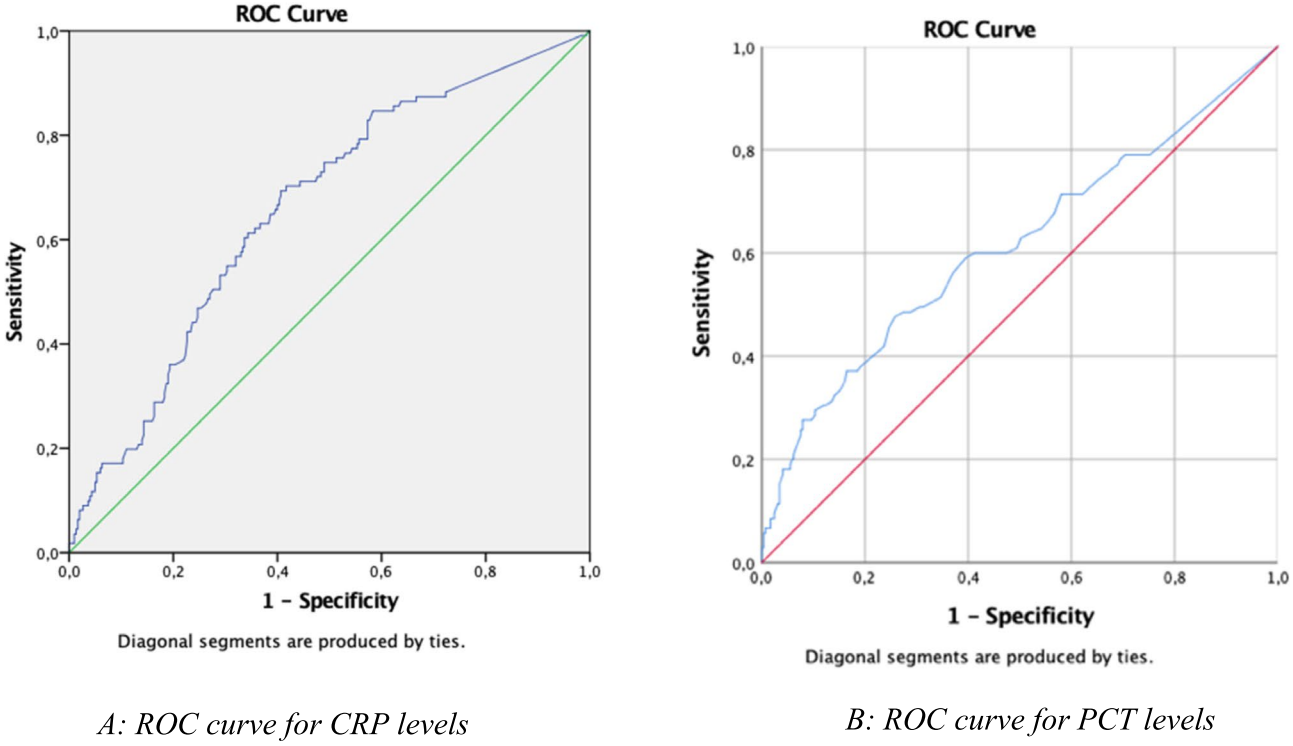
This study included a total of 411 patients. CRP analysis was conducted in 232 patients during the first trimester, 131 during the second trimester, and 131 during the third trimester. Procalcitonin analysis was performed in 228 patients during the first trimester, 117 during the second trimester, and 122 during the third trimester. Pregnancy loss occurred before 20 weeks of gestation in 14 patients. The mean age of the patients in our study was 29.8 years. The mean gravida was 2, and the mean parity was 0.7. The mean BMI, number of gestational weeks at the time of delivery and mean birth weight were 25.2, 38, 2 days, and 3131 g, respectively.

The incidence of composite obstetric complications was 27%, whereas composite neonatal complications occurred in 10.6% of cases. Gestational cholestasis was observed in five patients, and hypothyroidism was observed in eight patients. The incidence rates of specific complications among the study population were as follows: preterm labor (13.4%), PPROM (7.8%), IUGR (1.5%), preeclampsia (3.3%), gestational hypertension (2.7%), gestational diabetes mellitus (5.4%), gestational cholestasis (1.2%), hypothyroidism (1.9%), and pregnancy loss (3.4%).

The incidence rates of neonatal complications were as follows: respiratory distress syndrome (RDS) 1.9%,

Table 1 The mean CRP and PCT levels in relation to obstetric and neonatal complications

	CRP (No complication)	CRP (Complication)	*P* Value	PCT (No complication)	PCT (Complication)	*P* Value
Composite Obstetric Complications	9.07 ± 12.74	16.08 ± 23.95	0.000	0.04 ± 0.05	0.55 ± 3.53	0.013
Preeclampsia	10.93 ± 17.18	11.13 ± 5.73	0.967	0.17 ± 1.85	0.69 ± 2.13	0.355
GHT	10.62 ± 16.66	21.99 ± 22.83	0.028	0.19 ± 1.88	0.06 ± 0.04	0.839
GDM	10.84 ± 17.14	12.62 ± 13.00	0.632	0.19 ± 1.90	0.04 ± 0.02	0.728
IUGR	10.93 ± 17.04	11.47 ± 7.22	0.939	0.18 ± 1.87	0.06 ± 0.04	0.879
PPROM/Preterm labor	9.77 ± 12.90	18.95 ± 31.47	0.000	0.14 ± 1.83	0.41 ± 1.77	0.317
1 st trimester pregnancy loss	10.94 ± 16.93	11.58 ± 12.76	0.888	0.18 ± 1.85	0.04 ± 0.02	0.780
Composite Neonatal Complications	10.59 ± 17.19	13.76 ± 14.46	0.247	0.18 ± 1.93	0.23 ± 1.10	0.858
RDS	10.83 ± 17.07	12.65 ± 8.77	0.764	0.08 ± 0.56	1.06 ± 2.66	0.000
Neonatal Sepsis	10.52 ± 16.63	21.74 ± 22.98	0.019	0.08 ± 0.57	0.68 ± 2.03	0.002
NEC	-	-	-	-	-	-
The need for intensive care	10.60 ± 17.22	13.32 ± 14.30	0.321	0.18 ± 1.93	0.23 ± 1.10	0.859



A: ROC curve for CRP levels

B: ROC curve for PCT levels

Fig. 1 A: ROC curve for CRP levels - B: ROC curve for PCT levels

neonatal sepsis 1.2%, necrotizing enterocolitis (NEC) 0.2%, and intraventricular hemorrhage (IVH) 0.5%. The need for intensive care was observed in 10.5% of the patients.

The mean CRP level for all patients included in the study was 10.9 ± 16.7. The mean CRP levels in patients with and without obstetric complications were 16 ± 23.9 and 9 ± 12.7, respectively, indicating a statistically significant difference ($p = 0.004$). The mean procalcitonin level for all patients included in the study was 0.17 ± 1.8. The mean procalcitonin levels in patients with and without obstetric complications were 0.55 ± 3.52 and 0.04 ± 0.05, respectively, with no statistically significant difference ($p = 0.14$). The mean CRP and PCT levels in relation to obstetric and neonatal complications are summarized in Table 1.

The ROC curve was used to analyze the value of CRP values during pregnancy regardless of trimester to predict the presence of composite obstetric complications and revealed a cutoff value of 6.72 mg/L, with a sensitivity of 67% and specificity of 60% (Fig. 1- A). Similarly, the ROC curve was used to analyze the predictive value of PCT values during pregnancy for predicting obstetric complications and revealed a cutoff value of 0.0385 for a sensitivity of 60% and a specificity of 61%. This value was

Table 2 Clinical characteristics of patients with and without elevated CRP and PCT levels

	CRP ≤ 6.72	CRP > 6.72	*p* Value	PCT ≤ 0.0385	PCT > 0.0385	*p* Value
Age (years)	29.1 ± 4.9	30.7 ± 5.4	0.003	29.5 ± 5.1	29.8 ± 5.3	0.58
BMI(kg/m)^2	24.4 ± 3.7	26.0 ± 4.4	0.001	24.9 ± 4.1	25.4 ± 4.1	0.272
Birth Weight (g)	3169.4 ± 421.7	3089.4 ± 604.0	0.132	3175.6 ± 432.0	3073.9 ± 596.4	0.064
Gestational age at the time of delivery (weeks)	38.4 ± 1.5	38 ± 2.4	0.049	38.5 ± 1.7	37.9 ± 2.3	0.004

Table 3 Comparison of obstetric and neonatal outcomes in patients with and without elevated CRP and PCT

	CRP ≤ 6.72 *n* (%)	CRP > 6.72 *n* (%)	*P* Value	PCT ≤ 0.0385 *n* (%)	PCT > 0.0385 *n* (%)	*P* Value
Composite Obstetric Complications	36 (16.7%)	75 (38.3%)	0.001	43 (19.6%)	62 (34.8%)	0.001
Preeclampsia	2 (0.9%)	11 (5.9%)	0.006	4 (1.9%)	7 (4.1%)	0.225
GHT	0	11 (5.9%)	0.001	3 (1.4%)	6(3.6%)	0.191
GDM	9 (4.3%)	13 (7%)	0.237	11 (5.1%)	9 (5.3%)	0.936
IUGR	1 (0.5%)	5 (2.7%)	0.103	2 (0.9%)	3 (1.8%)	0.658
PPROM/Preterm labor	24 (11.2%)	30 (15.3%)	0.278	19(8.7%)	33 (18.6%)	0.003
1 st trimester pregnancy loss	4 (1.9%)	10 (5.1%)	0,07	5(2.3%)	9(5.1%)	0.136
Composite Neonatal Complications	15 (7.1%)	28 (14.5%)	0.017	15 (7%)	25(14.8%)	0.013
RDS	3(1.4%)	5 (2.7%)	0.481	1 (0.5%)	6 (3.6%)	0.047
Neonatal Sepsis	2(1%)	3(1.6%)	0.668	2(0.9%)	3(1.8%)	0.658
NEC	1(0.5%)	0	1	1(0.5%)	0	1
The need for intensive care	15(7.1%)	28(15.1%)	0.010	15(7%)	26(15.5%)	0.008

determined as the cutoff value for PCT to predict obstetric complications (Fig. 1-B).

The comparisons of demographic and obstetric data between those below and above the threshold values of CRP and PCT are shown in Table 1. The mean age and BMI of patients in the present study were significantly greater in those with CRP levels above the cutoff than in those with low CRP levels ($p = 0.003$ and $p = 0.003$, respectively). However, there was no statistically significant difference in birth weight between the two groups (Table 2). The mean age, BMI, and birth weight did not differ significantly between groups stratified by PCT levels above or below the cutoff (Table 2). In contrast, the mean gestational age at delivery was significantly greater in patients with low CRP and low PCT levels than in those with elevated CRP and PCT levels (Table 2).

A comparison of patients with and without elevated CRP levels in any trimester revealed a significantly greater frequency of composite obstetric complications in the elevated CRP group (32.4 – 67.6%) ($p < 0.001$) (Table 3). The frequencies of preeclampsia, gestational hypertension, neonatal complications and the need for intensive care were significantly greater in patients with CRP levels > 6.72 (Table 3). In addition, the prevalence of preeclampsia and the incidence of GHT were significantly greater in patients with elevated first trimester CRP levels ($p < 0.003$). No statistically significant differences were observed in the frequency of preterm labor, PPROM, IUGR, GDM or pregnancy loss in patients with elevated CRP above the cutoff (Table 3). The regression analysis indicated that only CRP elevation was a significant factor, while both age and BMI were not significant predictors of obstetric complications.

The incidence of composite obstetric complications was significantly greater in patients with elevated PCT (59% vs. 41%) ($p < 0.001$) (Table 3). No statistically significant difference was observed in the frequency of preeclampsia, gestational hypertension, IUGR, GDM, or pregnancy loss in patients with elevated PCT. However, patients with elevated PCT levels had a greater frequency of preterm labor or PPROM (18.6%), neonatal complications (14.8%), need for intensive care (15.5%), and RDS (3.6%) (Table 3).

Patients with elevated CRP levels had a 2.28-fold higher risk of experiencing any obstetric complication compared to those with lower CRP levels. This association was statistically significant (Reversed RR: 2.28; 95% CI: 1.62–3.24), indicating a strong relationship between systemic inflammation and adverse obstetric outcomes. Notably, there were the significant increases in the risk of preeclampsia (RR: 6.25; 95% CI: 1.40–27.78), composite neonatal complications (RR: 2.12; 95% CI: 1.17–3.85) and neonatal intensive care requirement (RR: 2.13; 95% CI: 1.17–3.86). Although the associations with GDM, pregnancy loss, IUGR, and neonatal sepsis did not reach statistical significance, clinically meaningful elevations in risk were observed. These findings suggest that maternal inflammation may substantially impact pregnancy outcomes and support the potential value of incorporating inflammatory markers, such as CRP, into obstetric risk assessment strategies. Obstetric and neonatal complications were significantly more frequent in pregnant

women with serum procalcitonin (PCT) levels ≥ 0.0385 ng/mL. The risk of developing composite obstetric complications was 1.77 times higher in the elevated PCT group compared to those with lower levels (RR: 1.77; 95% CI: 1.27–2.48). Notably, there was a marked increase in the risk of preterm delivery/PPROM (RR: 2.15; 95% CI: 1.27–3.65), neonatal sepsis (RR: 14.08; 95% CI: 1.83–108.33), and the need for neonatal intensive care (RR: 2.21; 95% CI: 1.29–3.78). This strong association between elevated PCT levels and adverse outcomes highlights the potential role of systemic inflammation in pregnancy complications and supports the utility of PCT as a possible early warning biomarker.

Discussion

This study revealed that the inflammatory markers CRP and procalcitonin may have predictive value in the prediction of some obstetric and neonatal complications. C-reactive protein is an acute-phase reactant synthesized by the liver in response to proinflammatory cytokines and is a sensitive index of systemic inflammation [2]. Previous studies have not consistently monitored CRP and procalcitonin levels across all three trimesters or examined the obstetric and neonatal outcomes associated with unexplained elevations of these markers. The strength of this study is its prospective design, which allowed for the systematic investigation of the relationships between CRP and procalcitonin levels and between CRP and neonatal outcomes. Additionally, we examined whether unexplained elevations in these inflammatory markers contribute to adverse pregnancy or neonatal complications, providing a comprehensive evaluation of both maternal and neonatal health.

Notably, the mean levels of CRP in healthy pregnant women appear to be higher than the standardized levels in people who are not pregnant. A study of CRP levels in healthy pregnant women without antepartum complications revealed that CRP levels measured serially from 22 weeks gestation until delivery ranged from 0.7 to 0.9 mg/dL, depending on gestational age, in women who did not give birth [19]. In our study, 6.72 mg/L was found to be the cutoff value for CRP for the incidence of obstetric and neonatal complications.

In a previous study, a procalcitonin threshold of 1.9 ng/mL was used, and the sensitivity and specificity of maternal serum procalcitonin levels for the early diagnosis of neonatal infection and histologic chorioamnionitis were reported to range from 53 to 75% and 45–45%, respectively [9]. In our study, we found that the predictive value of PCT levels during pregnancy for predicting obstetric complications was 0.0385 ng/mL, with a sensitivity of 60% and specificity of 61%.

C-reactive protein (CRP) has been investigated as a potential early biomarker for chorioamnionitis in women with premature rupture of membranes, as well as a predictor of outcomes in preterm labor. Spontaneous preterm labor is associated with a range of causal and contributing factors [20, 21]. In a study conducted by Lee et al., maternal serum CRP levels below 8 mg/dL demonstrated a high negative predictive value for early-onset neonatal sepsis and funisitis. Similarly, other studies have reported that low maternal CRP levels strongly indicate the absence of chorioamnionitis or neonatal infection [22, 23]. In the present study, no cases of chorioamnionitis were recorded, and no significant associations were found between CRP levels and preterm labor or PPROM. This lack of association may be attributed to the nonspecific nature of CRP and the multifactorial etiology of preterm labor.

Preeclampsia is a common complication of pregnancy, with clinical manifestations including hypertension, proteinuria, and end-organ damage due to endothelial dysfunction thought to be the result of a maternal inflammatory response [24–26]. Although systemic inflammation has been implicated in the pathogenesis of preeclampsia, it is not known whether elevated levels of C-reactive protein measured early in pregnancy are associated with the subsequent development of preeclampsia. In a recent study by Gencheva et al., 36 patients with gestational hypertension, 37 patients with preeclampsia and 50 patients were used as controls, and high-sensitivity CRP levels were compared between the 20th and 34th weeks of pregnancy. High-sensitivity CRP levels were significantly higher in the gestational hypertension group than in the control group, similar to the findings of our study. Although higher sensitivity CRP levels were observed in the preeclampsia group than in the control group [27]. In a recent study by Wolf et al. consisting of 40 preeclampsia and 80 control groups, CRP levels were found to be higher in the preeclampsia group (4.6 mg/L compared with 2.3 mg/L), similar to our study [6]. A systematic review concluded that high first-trimester CRP levels may increase the risk of preeclampsia, and measures such as aspirin initiation should be taken above 15 mg/L [28]. The mean CRP level was 16 mg/L in patients with obstetric complications in our study. In the studies by Cao et al. and Barden et al. investigating susceptibility to preeclampsia in women with GDM, CRP levels were found to be higher in the group that developed preeclampsia, suggesting that elevated CRP levels may be useful biomarkers for predicting the development of preeclampsia [29, 30]. In other studies, CRP levels were found to be significantly higher in patients with preeclampsia than in those with normal pregnancies [31–33]. In the present study, both preeclampsia and gestational hypertension were significantly more prevalent among patients with elevated levels of CRP and PCT, supporting the hypothesis that systemic

inflammation may play a role in the pathophysiology of hypertensive disorders during pregnancy. The significant increase in CRP and PCT levels in these groups suggests that these biomarkers could serve not only as reflections of an ongoing inflammatory response, but also as potential predictive indicators for the development of hypertensive complications. This finding aligns with previous studies that have identified inflammatory markers as contributors to endothelial dysfunction and vascular pathology in pregnancy-related hypertension. We recommend screening for CRP and procalcitonin, to help predict preeclampsia. However, further prospective studies are warranted to clarify the causal relationships and to evaluate their clinical utility in risk stratification and early intervention.

A study involving 450 women revealed that high-sensitivity CRP values in the first trimester are associated with the development of gestational diabetes mellitus later in pregnancy [34]. In a prospective study by Westergaard et al. including 1049 patients, there was no association between GDM and CRP levels [35]. In a study in which the cutoff value for CRP was set at 3 mg/dL, a significant increase in CRP was found in the group of patients with GDM compared with the control group [36]. In a Chinese study involving 36 GDM patients and 36 control groups, when fasting and 1 st hour CRP levels were measured during the OGTT, the levels were significantly greater in the GDM group than in the control group, suggesting that this difference was related to oxidative stress [37]. In our study, GDM was observed in a greater number of patients with elevated CRP in all trimesters, but this difference did not reach statistical significance. This may have been due to the small number of patients with GDM among the participants due to other risk factors.

In studies that have investigated the role of CRP in pregnancy loss, no association between high levels of CRP and pregnancy loss has been reported, similar to our study [38, 39]. Consequently, it is suggested that pregnancy loss is not associated with increased maternal systemic inflammation. In contrast, another study revealed that patients who experienced pregnancy loss had significantly higher CRP levels than patients with ongoing pregnancy and the control group did [40]. In our study, pregnancy loss was more common in patients with elevated CRP and procalcitonin levels, but no significant associations were found. Therefore, for the prediction of pregnancy loss, CRP and procalcitonin screening is not recommended.

Early detection of sepsis is critical to reduce morbidity and mortality and improve outcomes in infants with sepsis. Therefore, the availability of predictive tests for neonatal sepsis may be effective in clinical management. In a study of 25 patients with neonatal sepsis and 62 patients without sepsis, the mean maternal CRP protein levels of mothers with neonatal sepsis were significantly greater than those of control mothers [41]. In our study, there was no significant relationship between CRP or PCT and neonatal sepsis because of the small number of neonatal sepsis patients.

The incidence of composite neonatal complications and the need for neonatal intensive care increased significantly with elevated CRP and procalcitonin levels. According to our data, the highest need for intensive care is due to RDS. While procalcitonin elevation significantly increased RDS, no significant relationship was found between CRP elevation and RDS.

The limitation of this study is that, due to the prospective design, the number of patients with obstetric complications and neonatal complications in each group was inadequate for statistical significance. The CRP and PCT cut-off values derived from ROC curve analyses demonstrated relatively low sensitivity and specificity, which may limit their predictive utility.The number of patients whose CRP and PCT levels were analyzed in each trimester was low because of problems with patient follow-up.

Conclusions

In conclusion, elevated CRP and PCT are associated with increased obstetric and neonatal complications. CRP and PCT, which are inexpensive and available, may be used for screening to predict obstetric and neonatal complications during patient follow-up. This prospective study contributes to the existing literature by evaluating the relationship between CRP and PCT levels and obstetric and neonatal outcomes during pregnancy. This evalution is based on measurements obtained at multiple gestational time points. We recommend that the study be repeated with a larger number of patients for routine clinical use.

Abbreviations

BMI	Body mass index
CRP	C-reactive protien
IUGR	Intrauterine Growth Restriction
IVH	Intraventricular hemorrhage
GDM	Gestational diabetes mellitus
GHT	Gestational hypertension
NEC	Necrotizing enterocolitis
PCT	Procalcitonin
PROM	Premature Membrane Rupture
PPROM	Preterm premature rupture of membranes
ROC	Receiver operating characteristic

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Not applicable.

Authors' contributions

ME, PC and MA designed the study. MA, AGA, CY, and IMH collected the data. ME, PC and MA analyzed the data. MA drafted the work; PC, AE, and ME revised it substantially. All the authors read and approved the final manuscript.

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None.

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethical committee of the Gazi University Faculty of Medicine (Approval No:479). All patients who participated in the study were informed of the study, and informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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