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ASSOCIATION OF C - REACTIVE PROTEIN WITH PSYCHOTIC FEATURES IN POSTPARTUM DEPRESSION: A CROSS-SECTIONAL STUDY FROM PAKISTAN

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Abstract

Background: Postpartum depression (PPD) is one of the commonest psychiatric disorders following childbirth. PPD may be complicated by psychotic features, substantially increasing maternal morbidity and mortality. Increasing evidence suggests that inflammatory processes contribute to affective and psychotic symptoms. C-reactive protein (CRP), a widely available inflammatory marker, has been implicated in the etiology of depressive disorders, yet data linking CRP with psychotic features in PPD remain limited, particularly from low- and middle-income countries like Pakistan.

Objectives: To study the correlation between serum C-reactive protein levels and psychotic symptoms among women with postpartum depression.

Methods: This cross-sectional study was carried out at a tertiary care hospital in Hyderabad, Pakistan, over six months. A total of 236 postpartum women were enrolled using non-probability consecutive sampling. Postpartum depression was evaluated using the Urdu version of the Edinburgh Postnatal Depression Scale (EPDS), while psychotic symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS). Serum CRP levels were measured and categorized as normal (<5 mg/dL) or raised (≥5 mg/dL). Pearson correlation and logistic regression analyses were performed.

Results: The mean age of participants was 26.57 ± 5.87 years. Elevated CRP levels were observed in 47% of women. A significant positive correlation was found between CRP levels and psychotic symptom severity ($r = 0.63$, $p < 0.05$). Women with raised CRP had significantly higher odds of PPD with psychotic features (OR = 18.75; 95% CI: 9.68–36.30; $p = 0.0005$). After adjustment for sociodemographic and clinical variables, raised CRP remained an independent predictor (adjusted OR = 25.45; 95% CI: 11.76–55.06).

Conclusions: Elevated CRP levels are strongly associated with psychotic features in postpartum depression. These findings support the role of inflammation in the pathophysiology of severe postpartum mood disorders and highlight CRP as a potential biomarker for early identification of women at risk.

Keywords: Postpartum depression; psychotic features; C-reactive protein; inflammation; biomarker

Introduction

Postpartum depression (PPD) is a mental health condition characterized by depressive symptoms appearing within weeks to months after childbirth and affecting approximately 15–20% of women worldwide [1,2]. It reflects a major public health concern due to its adverse impacts on maternal and physical functioning, infant development, and an overall family well-being [3]. A particularly severe presentation is postpartum depression with psychotic features (like delusions, and hallucinations), which substantially enhances the risk of suicide and infanticide [4,5]. …..

Emerging evidence supports the inflammatory hypothesis of depression, suggesting that abnormalities in immune system and low-grade inflammation contribute to the onset and severity of affective and psychotic disorders [6,7]. increased circulating inflammatory markers, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), have been consistently revealed in individuals with major depressive disorder and psychosis-spectrum illnesses [8–10].

CRP is an acute-phase reactant synthesized by hepatocytes in response to pro-inflammatory cytokines and is widely used as a nonspecific marker of systemic inflammation [11]. Different studies have demonstrated an association between elevated CRP levels and severity of depressive symptom, treatment resistance, and cognitive impairments [12–14]. In perinatal psychiatry, physiological immune adaptations during pregnancy and immune rebound following delivery may predispose vulnerable women to exaggerated inflammatory responses, potentially triggering postpartum psychiatric especially mood disorders [15,16].

Physiological changes during pregnancy and after delivery involve significant hormonal withdrawal, hypothalamic–pituitary–adrenal (HPA) axis dysregulation, and immune system reactivation, all of which may interact resultining in increase in neuroinflammatory signaling [17–19]. These mechanisms are considered to contribute not only to depressive symptoms but also to the emergence of psychotic phenomena in the postpartum period [20].

Despite increasing international interest, data demonstrating the association between CRP and psychotic features in postpartum depression remain scarce, particularly from low- and middle-income countries like Pakistan [21]. Understanding biological correlates such as CRP may facilitate early identification of high-risk women and inform targeted monitoring and intervention strategies.

This study aimed to see the relationship between serum CRP levels and psychotic features among women with postpartum depression in a tertiary care setting in Pakistan.

Methods

Study Design and Setting

A cross-sectional study was conducted in the Department of Psychiatry at Civil Hospital Hyderabad, Pakistan, over a period of six months.

Participants

236 Postpartum women aged 18–45 years who consented to participate and were clinically suspected of having postpartum depression were included in the study. Women with a prior diagnosed psychiatric illness, neurological disorder, or significant medical comorbidity were exclusion criteria.

Measures

Postpartum depression was evaluated using the validated Urdu version of the Edinburgh Postnatal Depression Scale (EPDS), with a cutoff score of ≥11 indicating depression. Psychotic symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS). Serum CRP levels were measured using standard laboratory techniques and categorized as normal (<5 mg/dL) or raised (≥5 mg/dL).

Statistical Analysis

Data were analyzed using SPSS version 23. Continuous variables were summarized as mean ± standard deviation, while categorical variables were measured in frequencies and percentages. Pearson correlation analysis assessed the relationship between CRP levels and psychotic symptom severity. Logistic regression analyses were performed to identify predictors of PPD with psychotic features. A p-value ≤0.05 was considered statistically significant.

Results

Participant Characteristics

A total of 236 postpartum women were included in the study. The mean age was 26.57 ± 5.87 years, and the mean duration of marriage was 4.07 ± 2.30 years. Majority of the participants were multigravida (89%) and urban residents (73.3%). Raised CRP levels (≥5 mg/dL) were observed in 111 women (47%). Based on EPDS assessment, the prevalence of postpartum depression was found in 120 females (50.8%). (Table: 1)

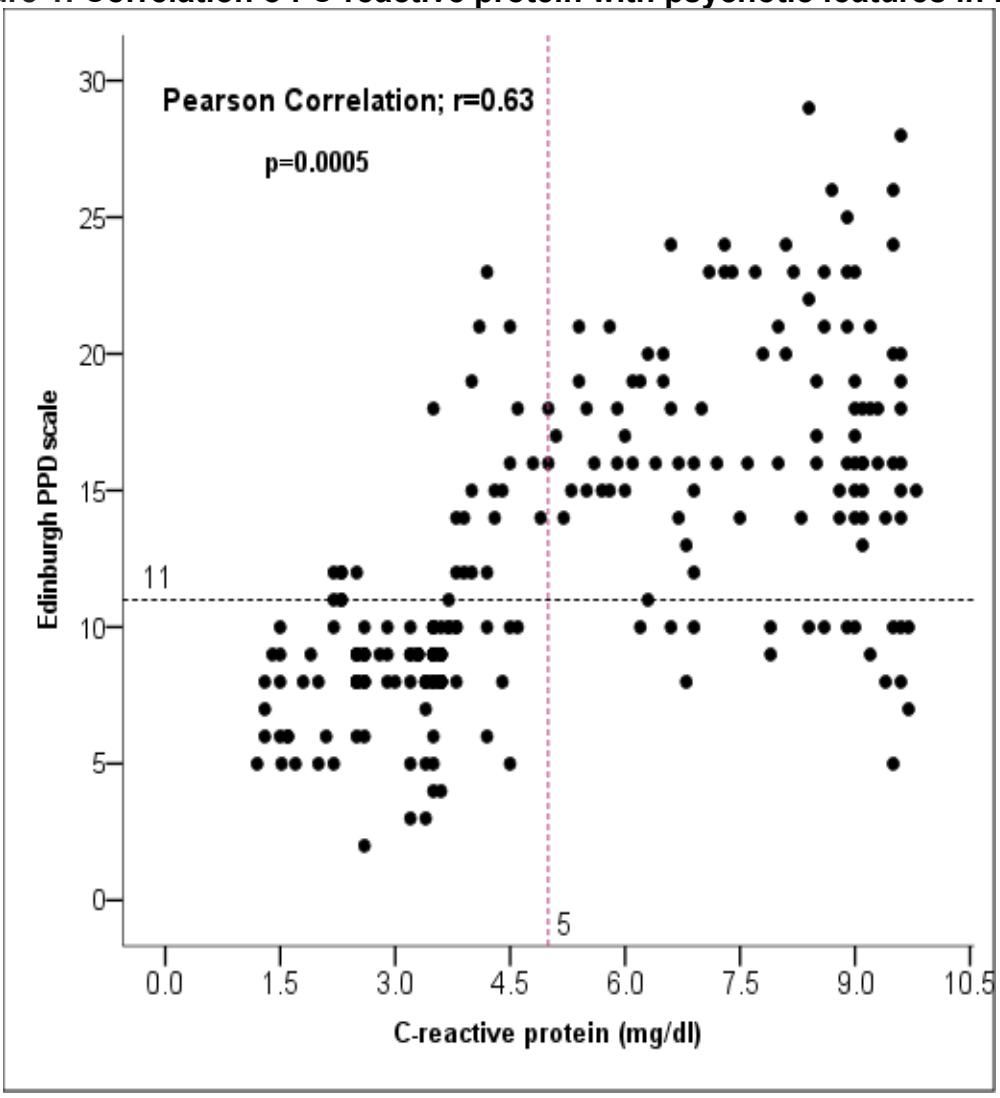
Table 1. Sociodemographic and Obstetric Characteristics of Participants (n = 236)

Variable	Category	n (%)
Age (years)	≤25	108 (45.8)
	>25	128 (54.2)
Residence	Urban	173 (73.3)
	Rural	63 (26.7)
Parity	Primigravida	26 (11.0)
	Multigravida	210 (89.0)
Education	Illiterate	72 (30.5)
	Primary–Secondary	104 (44.1)
	Higher education	60 (25.4)
Serum CRP level	Normal (<5 mg/dL)	125 (53.0)
	Raised (≥5 mg/dL)	111 (47.0)

Association o f C-reactive protein with psychotic features in postpartum depression

Pearson correlation of C-reactive protein with psychotic features in postpartum depression among women was positive and significant ($r=0.63$; $p<0.05$) indicating that higher inflammatory burden was associated with more severe psychotic manifestations. (Figure: 1)

Figure 1. Correlation o f C-reactive protein with psychotic features in PPD



Association Between CRP and Postpartum Depression

Categorical analysis showed that women with raised CRP levels were significantly more likely to have postpartum depression with psychotic features compared to those with normal CRP levels (OR = 18.75; 95% CI: 9.68–36.30; p = 0.0005). (Table: 2)

Table 2. Association Between Serum CRP Levels and Postpartum Depression with Psychotic Features

CRP Level	PPD with Psychotic Features n (%)	PPD without Psychotic Features n (%)	Odds Ratio (95% CI)	p-value
Normal (<5 mg/dL)	12 (9.6)	113 (90.4)	Reference	–
Raised (≥5 mg/dL)	68 (61.3)	43 (38.7)	18.75 (9.68–36.30)	0.0005

In multivariate logistic regression analysis adjusting for age, parity, residence, education, occupation, and socioeconomic status, elevated CRP remained an independent predictor of postpartum depression with psychotic features. (Table: 3)

Table 3. Multivariate Logistic Regression Analysis for Predictors of Postpartum Depression with Psychotic Features

Variable	Adjusted OR	95% CI	p-value
Raised CRP (≥5 mg/dL)	25.45	11.76–55.06	<0.001
Age (>25 years)	1.32	0.71–2.45	0.37
Multigravida status	1.18	0.52–2.67	0.69
Rural residence	1.41	0.76–2.62	0.27
Low education	1.89	0.98–3.64	0.06

Discussion

This study demonstrates a significant association between increased serum C-reactive protein (CRP) levels and psychotic features in postpartum depression. These findings are consistent with the growing body of evidence supporting the inflammatory hypothesis of mood and psychotic disorders, which explains that immune activation and low-grade systemic inflammation are contributory factors to the pathophysiology of severe psychiatric illnesses [6,7].

Previous research studies have consistently reported elevated CRP concentrations in individuals with major depressive disorder and in those with more severe or treatment-resistant features [10,12]. Meta-analytic data have further confirmed increased levels of inflammatory cytokines and acute-phase reactants in depression, strengthening the biological plausibility of our study's findings [8,9]. Our results extend this literature by specifically focusing on the postpartum period and the presence of psychotic features in depression, a comparatively underexplored yet clinically important dimension of postpartum psychopathology.

The postpartum period is marked by abrupt hormonal withdrawal, dysregulation of the hypothalamic–pituitary–adrenal axis, and a rebound activation of the immune system following pregnancy-induced immunotolerance [17–19]. These physiological changes may amplify inflammatory signaling susceptible women, thereby increasing vulnerability to severe affective (mood) disturbances with psychotic features [20].Raised CRP levels in our cohort may reflect this heightened inflammatory state, working as a peripheral marker of underlying neuroimmune dysregulation.

Findings of our study are consistent with those of prior studies reporting associations between inflammatory markers and postpartum depressive symptoms. Population-based data have shown that elevated CRP levels are associated with increased risk of postpartum depression, even after adjustment for sociodemographic and obstetric confounders [21]. Similarly, psychoneuroimmunological studies have demonstrated bidirectional interactions between inflammatory mediators and affective symptoms in the postpartum period, suggesting that inflammation may not only be a consequence but also a contributor to psychiatric morbidity [15,16, 21].

It is important to note that postpartum psychosis and depression with psychotic features are considered psychiatric emergencies due to their close association with suicide, infanticide, and severe functional impairment [4,5]. The identification of accessible biological markers such as CRP may therefore have important clinical implications. Routine assessment of inflammatory markers in high-risk postpartum women could potentially help early identification, risk stratification, and timely referral for specialist psychiatric care and prevention of the negative consequences.

While CRP is a nonspecific marker of inflammation, its widespread availability, relatively low cost, and ease of measurement make it a suitable candidate for integration into clinical screening frameworks, particularly in resource-limited settings [11]. Future studies incorporating longitudinal designs and broader panels of inflammatory cytokines are required to clarify causal pathways and establish whether anti-inflammatory interventions may play a role in the prevention or treatment of severe postpartum mood and other psychiatric disorders.

Strengths and Limitations

Strengths of this study include a relatively large sample size, use of validated assessment tools, and adjustment for multiple confounders. Limitations of the study include the cross-sectional design/setting, which precludes causal inference, and reliance on a single inflammatory marker. Longitudinal studies incorporating broader cytokine panels are required.

Conclusions

Elevated serum C-reactive protein is strongly associated with psychoticsymptoms in women with postpartum depression. CRP may serve as a simple and accessible biomarker to identify high-risk individuals who may benefit from early psychiatric evaluation, intervention, and intensive monitoring.

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