COMPARATIVE ANALYSIS OF INFLAMMATORY CYTOKINES IN PREGNANT WOMEN WITH AND WITHOUT PREECLAMPSIA

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Abstract
Preeclampsia is one of the most important hypertensive disorders of pregnancy associated with increased maternal and fetal complications. This hospital-based comparative cross-sectional study included 154 pregnant women (77 with preeclampsia and 77 healthy controls). Serum inflammatory biomarkers (PCT, CRP, IL-2, IL-6, IL-10, TNF-α, and IFN-α) were measured using enzyme-linked immunosorbent assay (ELISA).Women with preeclampsia exhibited significantly higher serum levels of all inflammatory biomarkers compared with healthy pregnant controls (IL-6: 18.42 ± 8.35 vs. 6.84 ± 3.21 pg/mL; CRP: 12.76 ± 5.18 vs. 4.32 ± 2.06 mg/L; both $p < 0.001$). Increased inflammatory cytokines, such as IL-6 and TNF-α, reflect increased systemic inflammation and immune dysfunction in preeclampsia. These findings may assist clinicians in identifying inflammatory alterations associated with preeclampsia and support future biomarker-based risk assessment strategies.

Keywords: Preeclampsia, Inflammatory Cytokines, IL-6, TNF-α, CRP, PCT, Pregnancy, Biomarkers.
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1. INTRODUCTION

Preeclampsia is defined as an elevated blood pressure (hypertension) and the presence of protein in the urine (proteinuria) after the 20th week of pregnancy. It is an important public health issue, especially in developing countries, and is a significant contributor to maternal and perinatal morbidity and mortality globally. Preeclampsia is a serious condition that affects about 2-8% of pregnancies, and has a large impact on the outcomes of both mothers and babies. Maternal complications are eclampsia, HELLP, renal failure, liver dysfunction, and cardiovascular complications while fetal complications are intrauterine growth restriction, preterm delivery, low birth weight, and perinatal death. Preeclampsia is a complex and multifactorial disease, characterized by abnormal development of the placenta and maternal systemic responses.

Inadequate trophoblastic invasion of the uterine spiral arteries results in impaired placental perfusion, placental ischemia, oxidative stress, and widespread endothelial dysfunction, which are central mechanisms in the pathogenesis of preeclampsia. During normal pregnancy, the immune activation is controlled and there is a dynamic balance between the pro-inflammatory and anti-inflammatory responses. Pre-eclampsia is, however, a pathological state that is associated with an excessive activation of the inflammatory cells and generation of inflammatory mediators. These inflammatory responses are mediated by cytokines and acute-phase proteins, which may be involved in the injury and the progress of the disease in the endothelium.

The association between preeclampsia and several inflammatory biomarkers has been studied, such as: Procalcitonin (PCT), C-Reactive Protein (CRP), Interleukin-2 (IL-2), Interleukin-6 (IL-6), Interleukin-10 (IL-10), Tumor Necrosis Factor-alpha (TNF-α), and Interferon-alpha (IFN-α). IL-6 and TNF-α are some of the important pro-inflammatory cytokines responsible for endothelial activation and vascular dysfunction, whereas IL-10 is an anti-inflammatory cytokine which might be elevated in response to an overactive inflammatory reaction. Increased levels of CRP and PCT have also been found in women with preeclampsia, which is indicative of the activation of systemic inflammatory processes. Although evidence is increasing, these biomarkers are not yet known to be predictive or clinically significant and results from various populations are conflicting.

In this regard, the present study was conducted to compare the concentration of inflammatory cytokines and related biomarkers in preeclamptic and normal pregnant women. The inflammatory profile of preeclampsia could facilitate the search for potential biomarkers for early diagnosis, disease monitoring and better maternal and foetal outcomes.

2. REVIEW OF LITERATURE

Laresgoiti-Servitje et.al (2013) Preeclampsia syndrome is characterized by inadequate placentation, because of deficient trophoblastic

invasion of the uterine spiral arteries, leading to placental hypoxia, secretion of proinflammatory cytokines, the release of angiogenic and antiangiogenic factors and miRNAs. Although immune-system alterations are associated with the origin of preeclampsia, other factors, including proinflammatory cytokines, neutrophil activation, and endothelial dysfunction, are also related to the pathophysiology of this syndrome. The pathophysiology of preeclampsia may involve several factors, including persistent hypoxia at the placental level and the release of high amounts of STBMs. DAMP molecules released under hypoxic conditions and STBMs, which bind TLRs, may activate monocytes, DCs, NK cells, and neutrophils, promoting persistent inflammatory conditions in this syndrome. The development of hypertension in preeclamptic women is also associated with endothelial dysfunction, which may be mediated by various mechanisms, including neutrophil activation and NET formation. Furthermore, preeclamptic women have higher levels of nonclassic and intermediate monocytes and lower levels of lymphoid BDCA-2^{+} DCs. The cytokines secreted by these cells may contribute to the inflammatory process and to changes in adaptive-immune system cells, which are also modulated in preeclampsia. The changes in T cell subsets that may be seen in preeclampsia include low Treg activity, a shift toward Th1 responses, and the presence of Th17 lymphocytes. B cells can participate in the pathophysiology of preeclampsia by producing autoantibodies against adrenoreceptors and autoantibodies that bind the AT1-R.

Deer, et.al (2023) Preeclampsia is a hypertensive disorder of major concern in pregnancy than can lead to intrauterine growth restriction, placental abruption and stillbirth. The pathophysiology of preeclampsia is multifactorial, including not only kidney dysfunction but also endothelial dysfunction, as the maternal endothelium becomes exposed to placental factors that are released into the circulation and increase systemic levels of vasoconstrictors, oxidative stress, anti-angiogenic factors and inflammatory mediators. Importantly, inflammation can lead to insufficient placental perfusion and low birthweight in offspring. Various innate and adaptive immune cells and mediators have been implicated in the development of preeclampsia, in which oxidative stress is associated with activation of the maternal inflammatory response. Immune cells such as regulatory T cells, macrophages, natural killer cells, and neutrophils are known to have major causative roles in the pathology of preeclampsia, but the contributions of additional immune cells such as B cells, inflammatory cytokines and anti-angiotensin II type 1 receptor autoantibodies are also now recognized. Immunological interventions, therefore, have therapeutic potential in this disease. Here, we provide an overview of the immune responses that are involved in the pathogenesis of preeclampsia, including the role of innate and adaptive immune cells and mediators.

Torres-Torres et.al (2024) Preeclampsia (PE) is a multifactorial pregnancy disorder characterized by hypertension and proteinuria, posing significant risks to both maternal and fetal health. Despite extensive research, its complex pathophysiology remains incompletely understood. This narrative review aims to elucidate the intricate mechanisms contributing to PE, focusing on abnormal placentation, maternal systemic response, oxidative stress, inflammation, and genetic and epigenetic factors. This review synthesizes findings from recent studies, clinical trials, and meta-analyses, highlighting key molecular and cellular pathways involved in PE. The review integrates data on oxidative stress biomarkers, angiogenic factors, immune interactions, and mitochondrial dysfunction. PE is initiated by poor placentation due to inadequate trophoblast invasion and improper spiral artery remodeling, leading to placental hypoxia. This triggers the release of anti-angiogenic factors such as soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng), causing widespread endothelial dysfunction and systemic inflammation. Oxidative stress, mitochondrial abnormalities, and immune dysregulation further exacerbate the condition. Genetic and epigenetic modifications, including polymorphisms in the Fms-like tyrosine kinase 1 (FLT1) gene and altered microRNA (miRNA) expression, play critical roles. Emerging therapeutic strategies targeting oxidative stress, inflammation, angiogenesis, and specific molecular pathways like the heme oxygenase-1/carbon monoxide (HO-1/CO) and cystathionine gamma-lyase/hydrogen sulfide (CSE/H2S) pathways show promise in mitigating preeclampsia's effects. PE is a complex disorder with multifactorial origins involving abnormal placentation, endothelial dysfunction, systemic inflammation, and oxidative stress. Despite advances in understanding its pathophysiology, effective prevention and treatment strategies remain limited. Continued research is essential to develop targeted therapies that can improve outcomes for both mothers and their babies.

Tanaka et.al (2018) Interleukin 6 (IL-6) is a prototypical cytokine for maintaining homeostasis. When homeostasis is disrupted by infections or tissue injuries, IL-6 is produced immediately and contributes to host defense against such emergent stress through activation of acute-phase and immune responses. However, dysregulated excessive and persistent synthesis of IL-6 has a pathological effect on, respectively, acute systemic inflammatory response syndrome and chronic immune-mediated

diseases. The IL-6 inhibitor, tocilizumab, a humanized anti-IL-6 receptor antibody, is currently being used for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, and Castleman disease. Lines of recent evidence strongly suggest IL-6 blockade can provide broader therapeutic strategy for various diseases included in acute systemic and chronic inflammatory diseases.

Mihara, et.al (2012) IL (interleukin)-6, which was originally identified as a B-cell differentiation factor, is a multifunctional cytokine that regulates the immune response, haemopoiesis, the acute phase response and inflammation. IL-6 is produced by various types of cell and influences various cell types, and has multiple biological activities through its unique receptor system. IL-6 exerts its biological activities through two molecules: IL-6R (IL-6 receptor) and gp130. When IL-6 binds to mIL-6R (membrane-bound form of IL-6R), homodimerization of gp130 is induced and a high-affinity functional receptor complex of IL-6, IL-6R and gp130 is formed. Interestingly, sIL-6R (soluble form of IL-6R) also binds with IL-6, and the IL-6–sIL-6R complex can then form a complex with gp130. The homodimerization of receptor complex activates JAKs (Janus kinases) that then phosphorylate tyrosine residues in the cytoplasmic domain of gp130. The gp130-mediated JAK activation by IL-6 triggers two main signalling pathways: the gp130 Tyr^{759}-derived SHP-2 (Src homology 2 domain-containing protein tyrosine phosphatase-2)/ERK (extracellular-signal-regulated kinase) MAPK (mitogen-activated protein kinase) pathway and the gp130 YXXQ-mediated JAK/STAT (signal transducer and activator of transcription) pathway. Increased IL-6 levels are observed in several human inflammatory diseases, such as rheumatoid arthritis, Castleman's disease and systemic juvenile idiopathic arthritis. IL-6 is also critically involved in experimentally induced autoimmune diseases. All clinical findings and animal models suggest that IL-6 plays a number of critical roles in the pathogenesis of autoimmune diseases. In the present review, we first summarize the IL-6/IL-6R system and IL-6 signal transduction, and then go on to discuss the physiological and pathological roles of IL-6.

Dhar, et.al (2021) SARS-CoV-2, an infectious agent behind the ongoing COVID-19 pandemic, induces high levels of cytokines such as IL-1, IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-γ etc in infected individuals that play a role in the underlying patho-physiology. Nonetheless, exact association and contribution of every cytokine towards COVID-19 pathology remains poorly understood. Delineation of the roles of cytokines during COVID-19 holds the key to efficient patient management in clinics. This study performed a comprehensive meta-analysis to establish association between induced cytokines and COVID-19 disease severity to help in prognosis and clinical care. Scientific literature was searched to identify 13 cytokines (IL-1β, IL-2, IL-2R, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-17, TNF-α and IFN-γ) from 18 clinical studies. Standardized mean difference (SMD) for selected 6 cytokines IL-2, IL-4, IL-6, IL-10, TNF-α and IFN-γ between severe and non-severe COVID-19 patient groups were summarized using random effects model. A classifier was built using logistic regression model with cytokines having significant SMD as covariates. Out of the 13 cytokines, IL-6 and IL-10 showed statistically significant SMD across studies synthesized. Classifier with mean values of both IL-6 and IL-10 as covariates performed well with accuracy of ~92% that was significantly higher than accuracy reported in literature with IL-6 and IL-10 as individual covariates. Simple panel proposed by us with only two cytokine markers can be used as predictors for fast diagnosis of patients with higher risk of COVID-19 disease deterioration and thus can be managed well for a favourable prognosis.

Ng, et.al (2009) Little is known about the immunopathogenesis of Chikungunya virus. Circulating levels of immune mediators and growth factors were analyzed from patients infected during the first Singaporean Chikungunya fever outbreak in early 2008 to establish biomarkers associated with infection and/or disease severity. Adult patients with laboratory-confirmed Chikungunya fever infection, who were referred to the Communicable Disease Centre/Tan Tock Seng Hospital during the period from January to February 2008, were included in this retrospective study. Plasma fractions were analyzed using a multiplex-microbead immunoassay. Among the patients, the most common clinical features were fever (100%), arthralgia (90%), rash (50%) and conjunctivitis (40%). Profiles of 30 cytokines, chemokines, and growth factors were able to discriminate the clinical forms of Chikungunya from healthy controls, with patients classified as non-severe and severe disease. Levels of 8 plasma cytokines and 4 growth factors were significantly elevated. Statistical analysis showed that an increase in IL-1β, IL-6 and a decrease in RANTES were associated with disease severity. This is the first comprehensive report on the production of cytokines, chemokines, and growth factors during acute Chikungunya virus infection. Using these biomarkers, we were able to distinguish between mild disease and more severe forms of Chikungunya fever, thus enabling the identification of patients with poor prognosis and monitoring of the disease.

Black, K. D., & Horowitz, J. A. (2018) Preeclampsia (PE), a serious and variable pregnancy complication affecting 5%–10% of the obstetric

population, has an undetermined etiology, yet inflammation is concomitant with its development, particularly in relation to endothelial dysfunction. The purpose of this systematic review was to examine the published evidence concerning an association between PE and inflammatory markers for their usefulness in the prediction or early identification of women with PE in antepartum clinical settings. In this systematic review, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The Cumulative Index for Nursing and Allied Health and MEDLINE/OVID were the electronic databases used for identifying published articles. We placed no time limit on the publication year. The search generated 798 articles. After removing duplicates, screening abstracts, and conducting full-text reviews, we retained 73 articles and examined 57 unique markers. This review shows that C-reactive protein and the cytokines, specifically the proinflammatory markers IL-6, IL-8, and tumor necrosis factor alpha, garner the most support as potential inflammatory markers for clinical surveillance of PE, particularly during the second and third trimesters. Based on this review, we cannot recommend any single inflammatory marker for routine clinical use to predict/identify PE onset or progression. Research is recommended to examine a combination panel of these four inflammatory markers both with and without clinical risk factors toward the goal of translation to practice.

Mohamed et.al (2025) Preeclampsia (PE) remains a leading cause of maternal and perinatal morbidity and mortality, with systemic inflammation playing a central role in its pathogenesis. Despite extensive research on inflammatory biomarkers, inconsistencies persist regarding their associations with disease severity and onset. This systematic review synthesizes current evidence on the relationship between inflammatory biomarkers and PE, focusing on their diagnostic and prognostic potential. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines, a comprehensive search was conducted across five databases (PubMed, Scopus, Web of Science, Embase, and CINAHL) to identify observational studies investigating inflammatory biomarkers in PE. Eligible studies included case-control, cross-sectional, and cohort designs with normotensive controls. Data extraction covered study characteristics, biomarker profiles, and clinical outcomes. Methodological quality was assessed using the Newcastle-Ottawa Scale. In total, 13 studies were included, predominantly from diverse geographical regions. Pro-inflammatory cytokines and acute-phase proteins (C-reactive protein) were consistently elevated in PE, with distinct profiles for early-onset (placental-driven inflammation) and late-onset (systemic inflammation) subtypes. Biomarkers such as neopterin and soluble urokinase-type plasminogen activator receptor showed promise in stratifying disease severity. Maternal-fetal inflammatory cascades were evident, with correlations between maternal biomarkers and adverse neonatal outcomes. However, heterogeneity in study designs, biomarker measurement timing, and inconsistent adjustments for confounders limited comparability. Quality assessment revealed seven low-risk and six moderate-risk studies, with no high-risk bias. Inflammatory biomarkers demonstrate significant associations with PE severity and onset, supporting their role in disease monitoring and risk stratification. However, methodological inconsistencies highlight the need for standardized protocols and larger, longitudinal studies to validate their clinical utility. Future research should integrate multi-omics approaches to refine biomarker panels and elucidate causal pathways, ultimately guiding targeted interventions.

RESEARCH GAPS

The literature reviewed has indicated that inflammation plays a major role in the pathogenesis of preeclampsia and some studies have shown that there is a variation in inflammatory cytokines and inflammatory markers like IL-6, CRP, and TNF-α. However, there is a lack of consistency in the findings on their diagnostic and prognostic value, and few studies have investigated the use of several inflammatory biomarkers together. In addition, data regarding the Indian population, especially from the eastern part of Uttar Pradesh, are lacking. Thus, the present study aimed to compare the levels of PCT, CRP, IL-2, IL-6, IL-10, TNF-α and IFN-α between pregnant women with and without preeclampsia to gain insight into the role of these cytokines in the prediction and severity of preeclampsia.

3. AIM AND OBJECTIVES

Aim

To evaluate the association between inflammatory biomarkers and preeclampsia among pregnant women attending a tertiary care teaching hospital in Lucknow, Uttar Pradesh, India.

Objectives

- To estimate and compare serum levels of PCT, CRP, IL-2, IL-6, IL-10, TNF-α, and IFN-α in women with preeclampsia and healthy pregnant controls.
- To evaluate the association between inflammatory biomarker levels and the occurrence of preeclampsia.

- To determine the relationship between biomarker levels and the severity of preeclampsia.
- To compare the inflammatory biomarker profile between women with preeclampsia and healthy pregnant controls.

4. MATERIALS AND METHODS

Study Design

The present study was designed as a hospital-based comparative cross-sectional study conducted to evaluate and compare inflammatory cytokine levels among pregnant women with preeclampsia and healthy normotensive pregnant women.

Study Setting

The study was carried out in the Department of Obstetrics and Gynecology in collaboration with the Department of Biochemistry at a tertiary care teaching hospital in Eastern Uttar Pradesh, India. The study was conducted after obtaining approval from the Institutional Ethics Committee.

Study Population

The study population consisted of antenatal women attending the Obstetrics and Gynecology outpatient and inpatient departments of the study hospital.

Gestational Age Range

Pregnant women with a gestational age of 20 weeks or more were included in the study.

Sample Size

The sample size was calculated using the formula for comparison of two independent means:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 (\sigma_1^2 + \sigma_2^2)}{d^2}$$

Where:

- n = required sample size per group
- $Z_{\alpha/2}$= 1.96 for 95% confidence interval
- Z_{β}= 0.84 for 80% power
- σ= standard deviation
- d = expected difference between means

Based on previous studies and allowing for possible attrition, a total sample size of 154 participants was included, comprising 77 cases and 77 controls.

Study Groups

Preeclampsia Group

This group included 77 pregnant women diagnosed with preeclampsia according to the American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 222 (2020). Women were diagnosed with new-onset hypertension (blood pressure ≥140/90 mmHg) after 20 weeks of gestation accompanied by proteinuria.

Healthy Pregnant Women (Control) Group

This group included 77 healthy normotensive pregnant women matched for gestational age and maternal age, without evidence of proteinuria or any major pregnancy-related complications.

Inclusion Criteria

- Pregnant women aged 18–40 years.
- Gestational age ≥20 weeks.
- Women diagnosed with preeclampsia (case group).
- Healthy normotensive pregnant women (control group).
- Willingness to participate and provide written informed consent.

Exclusion Criteria

- Chronic hypertension.
- Diabetes mellitus.
- Chronic renal disease.
- Autoimmune disorders.
- Acute or chronic infections.
- Multiple pregnancy.
- Premature rupture of membranes.
- Placental abruption.
- History of immunosuppressive therapy.

- Refusal to provide informed consent.

Blood Sample Collection

Approximately 5 mL of venous blood was collected from each participant under aseptic conditions from the antecubital vein. Samples were collected in sterile vacutainer tubes and transported immediately to the laboratory for processing.

Plasma Separation and Storage

Blood samples were centrifuged at 3000 rpm for 10 minutes. The separated **serum** was carefully transferred into sterile cryovials and stored at **−80°C** for up to **3 months** until further biochemical analysis.

ELISA Method for Cytokine Estimation

Serum levels of Procalcitonin (PCT), C-Reactive Protein (CRP), Interleukin-2 (IL-2), Interleukin-6 (IL-6), Interleukin-10 (IL-10), Tumor Necrosis Factor-alpha (TNF-α), and Interferon-alpha (IFN-α) were estimated using commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kits (Elabscience Biotechnology Inc., Wuhan, China) according to the manufacturer's instructions.

Briefly, standards and serum samples were added to antibody-coated microplate wells and incubated under controlled conditions. Following washing steps, enzyme-conjugated detection antibodies and substrate solutions were added. Optical density was measured at 450 nm using an ELISA microplate reader, and cytokine concentrations were calculated from standard calibration curves.

Quality-Control Procedures: All serum samples were analyzed in duplicate according to the manufacturer's protocol. Standards, blanks, and quality-control samples were included in each assay run. The average value of duplicate measurements was used for statistical analysis, and assays with a coefficient of variation greater than 10% were repeated to ensure analytical accuracy and reproducibility.

Data Collection Procedure

A structured proforma was used to collect demographic, clinical, and laboratory information from all participants. Data collected included maternal age, gravidity, parity, gestational age, body mass index (BMI), blood pressure measurements, proteinuria status, and inflammatory biomarker levels. All information was recorded confidentially and maintained in secure study records.

Statistical Analysis Using SPSS

The collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. **The normality of continuous variables was assessed using the Shapiro–Wilk test.** Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.

Comparisons between the two groups were performed using the Independent Student's t-test for continuous variables and the Chi-square test for categorical variables. A p-value less than 0.05 was considered statistically significant. The results were presented in the form of tables, graphs, and descriptive statistical summaries.

5. RESULTS

A total of 154 pregnant women were enrolled, including 77 women with preeclampsia and 77 healthy normotensive pregnant women who served as controls.

Table 5.1 presents the demographic and clinical characteristics of the study participants. The average age of the mothers was 28.4 ± 4.8 years in the preeclampsia group and 27.9 ± 4.5 years in the control group. There was no significant difference in age of the mother ($p = 0.521$). Likewise, gestational age during enrollment was similar for the two groups (33.7 ± 2.8 weeks vs. 34.1 ± 2.6 weeks; $p = 0.372$). There was also no significant difference between the two groups in terms of parity. (62.3% in preeclampsia group and 55.8% in control group, $p = 0.412$). But BMI was significantly higher in the women with preeclampsia than in the controls (29.1 ± 3.6 kg/m² versus 25.8 ± 3.1 kg/m²; $p < 0.001$).

Table 5.1 Demographic and Clinical Characteristics of Study Participants

Variables	Preeclampsia (n=77)	Controls (n=77)	p-value
Maternal Age (years)	28.4 ± 4.8	27.9 ± 4.5	0.521
BMI (kg/m²)	29.1 ± 3.6	25.8 ± 3.1	<0.001 *
Gestational Age (weeks)	33.7 ± 2.8	34.1 ± 2.6	0.372
Primigravida, n (%)	48 (62.3)	43 (55.8)	0.412

Multigravida, n (%)	29 (37.7)	34 (44.2)	—

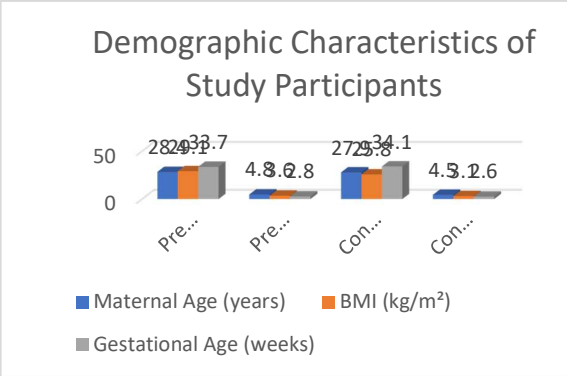

Figure 1: Demographic Characteristics of Study Participants

The results of the comparison of inflammatory biomarkers between the two groups are displayed in Table 5.2. Women with preeclampsia had significantly higher serum levels of Procalcitonin (PCT), C-Reactive Protein (CRP), Interleukin-2 (IL-2), Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-α) and Interferon-alpha (IFN-α) than healthy pregnant controls ($p < 0.001$ in all comparisons). Of all inflammatory markers measured, IL-6 had one of the greatest differences between groups.

The mean IL-6 concentration was 18.42 ± 8.35 pg/mL in women with preeclampsia compared with 6.84 ± 3.21 pg/mL in controls ($p < 0.001$). Likewise, the levels of CRP were also significantly higher in the preeclampsia group (12.76 ± 5.18 mg/L) than in controls (4.32 ± 2.06 mg/L; $p < 0.001$). Women with preeclampsia also exhibited significantly higher serum IL-10 levels, suggesting activation of compensatory anti-inflammatory mechanisms.

The increased inflammatory and immune activation, characteristic of disease pathogenesis, was reflected by the significantly elevated levels of TNF-α and IFN-α in the preeclampsia group.

Table 5.2 Comparison of Inflammatory Biomarkers Between Study Groups

Biomarker	Preeclampsia (n=77)	Controls (n=77)	p-value
PCT (ng/mL)	1.82 ± 0.74	0.48 ± 0.21	<0.001 *
CRP (mg/L)	12.76 ± 5.18	4.32 ± 2.06	<0.001 *
IL-2 (pg/mL)	14.28 ± 6.54	7.15 ± 3.12	<0.001 *
IL-6 (pg/mL)	18.42 ± 8.35	6.84 ± 3.21	<0.001 *
IL-10 (pg/mL)	8.91 ± 3.47	5.12 ± 2.11	<0.001 *
TNF-α (pg/mL)	22.64 ± 9.18	9.47 ± 4.26	<0.001 *
IFN-α (pg/mL)	15.73 ± 6.82	6.25 ± 2.88	<0.001 *

The findings demonstrated a significantly enhanced inflammatory response among women with preeclampsia compared with healthy pregnant controls, as evidenced by elevated concentrations of both pro-inflammatory cytokines and acute-phase reactants.

6. DISCUSSION

The present study demonstrated significantly elevated serum concentrations of PCT, CRP, IL-2, IL-6, IL-10, TNF-α, and IFN-α in women with preeclampsia compared with healthy pregnant controls. The results confirm the hypothesis that systemic inflammation is a key factor in the mechanism of preeclampsia. An increase in pro-inflammatory cytokines like IL-6 and TNF-α may be responsible for endothelial dysfunction, abnormal vascular responses and poor placental perfusion which cause the clinical symptoms of the disease. The findings are similar to those of previous studies which have found increased inflammatory activity in preeclamptic pregnancies. Our findings are consistent with recent evidence reported by Deer et al. (2023), who highlighted the central role of immune dysregulation and inflammatory cytokines in the development of preeclampsia. Similarly, Torres-Torres et al. (2024) reported that placental hypoxia and endothelial dysfunction promote increased production of pro-inflammatory cytokines, including IL-6 and TNF-α. Furthermore, the systematic review by Mohamed et al. (2025) concluded that inflammatory biomarkers are significantly associated with disease severity and may contribute to improved risk stratification in women with preeclampsia.

Although IL-10 is an anti-inflammatory cytokine, its increased concentration in women with

preeclampsia may represent a compensatory regulatory response aimed at limiting excessive inflammation. Despite this increase, the anti-inflammatory response appears insufficient to counterbalance the heightened pro-inflammatory state characteristic of preeclampsia. A major strength of the present study is the simultaneous evaluation of multiple inflammatory biomarkers, including pro-inflammatory cytokines, anti-inflammatory cytokines, and acute-phase reactants in the same study population. The use of a matched control group and standardized ELISA-based estimation further enhanced the reliability of the findings. However, the single-center design and relatively modest sample size may limit the generalizability of the findings.

The study was conducted at a single tertiary care center with a relatively modest sample size, which may limit the generalizability of the findings. In addition, inflammatory biomarkers were measured at a single time point, and no receiver operating characteristic (ROC) analysis was performed to determine diagnostic cut-off values. Future multicenter prospective studies with larger sample sizes are recommended to validate these findings.

7. CONCLUSION

The study concluded that pregnant women with preeclampsia have significantly elevated levels of inflammatory biomarkers, including PCT, CRP, IL-2, IL-6, IL-10, TNF-α, and IFN-α, compared to healthy pregnant women. These findings provide further evidence that systemic inflammation plays a pivotal role in the pathogenesis of preeclampsia. IL-6 and TNF-α, together with CRP and PCT, appear to be promising biomarkers as biomarkers for the early diagnosis and assessment of disease severity.

REFERENCES

1. Black KD, Horowitz JA. Inflammatory markers and preeclampsia: a systematic review. Nurs Res. 2018;67(3):242-251. doi:10.1097/NNR.0000000000000271.
2. Wang X, Wang T, Wang J, Niu X, Wang K, Hao Z, et al. Circulating transforming growth factor-β1 levels in preeclamptic women: a meta-analysis. Reprod Sci. 2023;30(6):1952-1964. doi:10.1007/s43032-022-01156-x.
3. Kuczma MP, Szurek EA, Cebula A, et al. Commensal epitopes drive differentiation of colonic Tregs. Sci Adv. 2020;6(16):eaaz3186. doi:10.1126/sciadv.aaz3186.
4. Yusrawati Y, Aidina D, Yerizel E. Comparison of transforming growth factor-beta 1 concentration in preeclampsia and normal pregnancy women. Indones Biomed J. 2017;9(1):49-54.
5. Teles A, Schumacher A, Kühnle MC, et al. Control of uterine microenvironment by Foxp3+ cells facilitates embryo implantation. Front Immunol. 2013;4:158. doi:10.3389/fimmu.2013.00158.
6. Stefańska K, Zieliński M, Jankowiak M, et al. Cytokine imprint in preeclampsia. Front Immunol. 2021;12:667841. doi:10.3389/fimmu.2021.667841.
7. Deer E, Herrock O, Campbell N, Cornelius DC, Fitzgerald S, Amaral LM, et al. The role of immune cells and mediators in preeclampsia. Nat Rev Nephrol. 2023;19(4):257-270. doi:10.1038/s41581-022-00672-7.
8. Dhar SK, Vishnupriyan K, Damodar S, Gujar S, Das M. IL-6 and IL-10 as predictors of disease severity in COVID-19 patients: results from meta-analysis and regression. Heliyon. 2021;7(2):e06155. doi:10.1016/j.heliyon.2021.e06155.
9. Areda BG, Gizaw ST, Berdida DH, Kebalo AH. Evaluation of serum lipid profiles, uric acid, and high sensitivity C-reactive protein levels between pregnancy-induced hypertension and normotensive pregnant women attending Ambo University Referral Hospital, Ethiopia: a case-control study. Health Sci Rep. 2022;5(5):e806. doi:10.1002/hsr2.806.
10. Sakaguchi S, Sakaguchi N, Asano M, Itoh M, Toda M. Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). J Immunol. 1995;155(3):1151-1164.
11. Hsu P, Nanan RK. Innate and adaptive immune interactions at the fetal-maternal interface in healthy human pregnancy and pre-eclampsia. Front Immunol. 2014;5:125. doi:10.3389/fimmu.2014.00125.
12. Laresgoiti-Servitje E. A leading role for the immune system in the pathophysiology of preeclampsia. J Leukoc Biol. 2013;94(2):247-257. doi:10.1189/jlb.1112603.
13. Koucký M, Malíčková K, Cindrová-Davies T, et al. Low levels of circulating T-regulatory lymphocytes and short cervical length are associated with preterm labor. J Reprod Immunol. 2014;106:110-117. doi:10.1016/j.jri.2014.04.001.
14. Mihara M, Hashizume M, Yoshida H, Suzuki M, Shiina M. IL-6/IL-6 receptor system and its role in physiological and pathological conditions. Clin Sci (Lond). 2012;122(4):143-159. doi:10.1042/CS20110340.

15. Mohamed RHA, Alfaki NMAA, Belal RE, Dawelbait AMA, Yousif RBH, Mohamed SA, et al. Biomarkers of inflammation and their association with the severity and onset of preeclampsia: a systematic review. Cureus. 2025;17(7):e91718. doi:10.7759/cureus.91718.
16. Ballesteros A, Mentink-Kane MM, Warren J, Kaplan GG, Dveksler GS. Induction and activation of latent transforming growth factor-β1 are carried out by two distinct domains of pregnancy-specific glycoprotein 1 (PSG1). J Biol Chem. 2015;290(7):4422-4431. doi:10.1074/jbc.M114.597518.
17. Li X, Shen L, Tan H. Polymorphisms and plasma level of transforming growth factor-beta 1 and risk for preeclampsia: a systematic review. PLoS One. 2014;9(5):e97230. doi:10.1371/journal.pone.0097230.
18. Care AS, Bourque SL, Morton JS, Hjartarson EP, Robertson SA, Davidge ST. Reduction in regulatory T cells in early pregnancy causes uterine artery dysfunction in mice. Hypertension. 2018;72(1):177-187. doi:10.1161/HYPERTENSIONAHA.118.10858.
19. Tanaka T, Narazaki M, Kishimoto T. Interleukin (IL)-6 immunotherapy. Cold Spring Harb Perspect Biol. 2018;10(8):a028456. doi:10.1101/cshperspect.a028456.
20. Torres-Torres J, Espino-y-Sosa S, Martinez-Portilla RJ, Borboa-Olivares H, Estrada-Gutierrez G, Acevedo-Gallegos S, et al. A narrative review on the pathophysiology of preeclampsia. Int J Mol Sci. 2024;25(14):7569. doi:10.3390/ijms25147569.