Assessment of Interleukin-6, Tumor Necrosis Factor-Α and C-Reactive Protein in Preeclamptic Women in Nasarawa State Nigeria

**Abstract**

**Background:** Pre-eclampsia is a life-threatening high blood pressure disorder which usually develops after 20 weeks of pregnancy affecting both the mother and the unborn child. Globally, it is estimated that over 70,000 maternal deaths and 500,00 fetal deaths occur annually due to preeclampsia. Majority of these deaths are recorded in low and middle-income countries. **Objective:** This study focused on the assessment of the levels of inflammatory cytokines (Interleukin-6, Tumor Necrosis Factor-α and C-Reactive Protein) among preeclamptic women in Nasarawa State and to determine the relationship between these markers and the onset of preeclampsia.

**Study Design:** The current study was a cross-sectional study

**Place and Duration of Study:** This study was carried out in selected hospitals in Nasarawa State, Nigeria from June 2024 to September 2024.

**Methodology:** Fifty twoblood samples were collected from preeclamptic women and normotensive controls into Ethylene Diamine Tetraacetic Acid (EDTA) tubes, spun at 3000 rpm for 10 minutes before collecting the plasma into labeled tubes and stored at -20oC until ready for analysis. The preeclamptic women ≤34 weeks pregnant were selected based on having blood pressure of 140/90, having protein in their urine, and reside within the study area. The control group were normotensive, without proteinuria. Interleukin-6, Tumor Necrosis Factor-α and C-Reactive Protein were estimated using ELISA method. Urine samples were also collected from both groups for protein detection using dipstick method. Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSSv23.0). Continuous variables were reported as mean ± SD, with comparison using the independent t- test and correlations assessed with the Pearson/Spearman coefficients (P<0.05).

**Results:** There weresignificantly elevated levels of all three inflammatory markers in the preeclamptic group. Mean IL-6 levels were 48.7 ± 12.3 pg/mL in preeclamptic women versus 18.2 ± 5.6 pg/mL in controls (*P*< 0.05). Similarly, TNF-α levels were 35.4 ± 10.7 pg/mL in preeclamptic women compared to 16.9 ± 4.8 pg/mL in normotensive women (*P*< 0.05). CRP levels were also markedly higher in the preeclamptic group 16.2 ± 5.9 mg/L than in controls 5.7 ± 2.4 mg/L (*P*< 0.05). Correlation analyses revealed strong positive associations between CRP and IL-6 (r = 0.68, *P*< 0.05) and between CRP and TNF-α (r = 0.61, *P*< 0.05).

**Conclusion:** This study revealed elevated levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) among the study participants. There is need to include the estimation of these inflammatory markers in routine antenatal test in addition to existing test especially among women most at risk of preeclampsia.

**Keywords:** Maternal mortality, Preeclampsia, Pregnancy, Interleukin-6, Tissue Necrotic Factor-α, C-reactive Protein

**Introduction**

The World Health Organization (WHO) describes Pre-eclampsia as a life-threatening high blood pressure disorder which usually develops after 20 weeks of pregnancy. Mothers and their unborn babies face a serious risk from this condition (WHO, 2025a). Globally, maternal mortality associated with complications due to preeclampsia comes second behind haemorrhage. In 2023 alone, over 700 women died daily from pregnancy and childbirth-related complications that are preventable (WHO, 2025b). About 87% of these deaths occurred in sub-Saharan Africa and southern Asia, with sub-Saharan Africa alone accounting for 80% of the deaths. Nigeria is reported to have the highest estimated maternal mortality rate of 28.3% of all global maternal deaths, accounting for approximately 8200 maternal deaths. (WHO, 2023a; Dogbanya, 2025). Due to its complexity and diverse presentations, pre-eclampsia can be difficult to diagnose and manage effectively. There is a consensus that a dysfunctional placenta, which releases factors into the pregnant woman’s bloodstream, causes systemic inflammation and widespread maternal endothelial dysfunction. It is often associated with at least one other complication, including proteinuria, maternal organ dysfunction or uteroplacental dysfunction. It is classified as preterm, term and postpartum preeclampsia (Dimitriadis *et al*., 2023; WHO, 2023b; Ngene & Moodley, 2024).

Inflammatory cytokines play a central role in the development of preeclampsia. Pro-inflammatory cytokines such as Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-α), and Interleukin-8 (IL-8) are markedly elevated in preeclamptic women. IL-6, a key mediator of inflammation, is associated with vascular inflammation and endothelial damage, while TNF-α exacerbates endothelial dysfunction and contributes to hypertension (Yao *et al*., 2019; Spence *et al*., 2021). Conversely, anti-inflammatory cytokines such as IL-4 and IL-10 help regulate the inflammatory response by attenuating pro-inflammatory cytokine production and reducing blood pressure (Rodriguez-Iturbe *et al*., 2016; Pioli *et al*., 2019). C-Reactive Protein (CRP), a biomarker of systemic inflammation, is also significantly elevated in preeclampsia and correlates with disease severity (Kusama *et al*., 2024; Oyeyinka & Olaniyan, 2024). It contributes to endothelial dysfunction and oxidative stress, further exacerbating the condition. The imbalance between pro-inflammatory and anti-inflammatory cytokines, along with elevated CRP levels, creates a pro-inflammatory state that drives the pathogenesis of preeclampsia (Maio *et al*., 2020; Petkova-Parlapanska *et al*., 2025). Preeclampsia and eclampsia account for a significant proportion of maternal mortality in Nigeria, accounting for up to 20–40% of all maternal deaths in tertiary healthcare settings with prevalence ranging from 2% to 16.7% (Adamu *et al*., 2020; Akaba *et al*., 2021). In Nasarawa State, Nigeria, preeclampsia remains a significant public health challenge, contributing to high rates of maternal and neonatal morbidity and mortality (Okonofua *et al*., 2020). Factors such as limited access to healthcare, poor antenatal care, high prevalence of infectious diseases, and nutritional deficiencies may exacerbate the inflammatory response in pregnant women, increasing their risk of developing preeclampsia (Ugwu *et al*., 2019; Kinshella *et al*., 2022; Dimitriadis *et al*., 2023). Understanding the local burden of pre-eclampsia and the role of inflammatory markers in this population is critical for developing targeted interventions to reduce its impact.

The objective of this study was to assess the levels of inflammatory cytokines (IL-6, TNF-α) and CRP in pre-eclamptic women in Nasarawa State and to determine the relationship between these markers and the onset of preeclampsia. By comparing these levels to those of normotensive pregnant women, the study aimed to provide insights into the role of inflammation in pre-eclampsia and inform strategies for early detection and management.

**Materials and Methods**

**Study Location and Population**

Nasarawa State is located in the middle belt region of north Central Nigeria with coordinates 8o32’N and 8o18’E. It has a population of 2.5 million based on the 2006 population census and a total area of 27,1117km2 (10,470sqm) comprising 13 local Government areas. It is bounded in the north by Kaduna State, in the west by Abuja (FCT), in the south by Kogi and Benue and in the east by Taraba and Plateau States. It lies within the guinea savannah region and has a tropical climate (Figure 1) (Akwa, 2007). The study participants were pregnant women with pre-eclampsia and normotensive (controls) attending ante-natal clinics of some government owned healthcare centers in Nasarawa State.



Fig:1 Map of Nasarawa State (Agidi, *et al., 2018*).

**Inclusion and exclusion criteria**

Women with pregnancies ≤34 weeks gestational age, with a blood pressure of 140/90, having protein in their urine and access antenatal care in selected hospitals in the study with absence of labor and premature rupture of membranes were selected.

**Exclusion Criteria**

Pregnant women with history of diabetes mellitus, cardiovascular diseases, Sickle cell disease, symptomatic infection diseases, women in labor and those with eclampsia were excluded. Also, those who didn’t give consent for the study were excluded.

 **Sample Size Determination**

The sample size was calculated using the comparative two-group mean formula for case-control studies (Charan & Biswas, 2013):

n=2(Zα/2+Zβ)2×σ2Δ2*n*=Δ22(*Zα*/2​+*Zβ*​)2×*σ*2​

Where:

Zα/2*Zα*/2​ = 1.96 (95% confidence level)

Zβ*Zβ*​ = 0.84 (80% power)

σ*σ* = 2.8 mg/L (pooled SD from Ugwu *et al*., 2021)

ΔΔ = 2.5 mg/L (clinically significant CRP difference)

Parameter Justification

1. Standard Deviation (σ):

Derived from Nigerian PE studies:

PE group: 3.2 mg/L

Controls: 1.1 mg/L

Pooled SD = 2.8 mg/L (conservative estimate)

1. Effect Size (Δ):
	1. mg/L difference represents:
	2. 2× control group mean CRP

Threshold for clinical significance (NICE, 2021)

1. Statistical Power:

80% power is acceptable for exploratory biomarker studies

Aligns with WHO minimum recommendations (2022)

Final Calculation

n=2(1.96+0.84)2×2.822.52=19.6≈20 per group*n*=2.522(1.96+0.84)2×2.82​=19.6≈20 per group

With adjustments:

15% attrition → 24/group

Total N = 48 → Rounded to 52 (26 cases/26 controls) for balanced design and minor protocol deviations.

Validation of adequacy

This sample size can detect:

IL-6 differences ≥15 pg/mL (80% power, SD=12 pg/mL)

TNF-α differences ≥10 pg/mL (SD=8 pg/mL)

Matches similar Nigerian biomarker studies (Okonofua *et al*., 2021).

**Data Analysis**

Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSSv23.0). Continuous variables were reported as mean ± SD, Comparison used the independent t- test while correlations were assessed with the Pearson/Spearman coefficients (P < 0.05).

**Sample Collection and Storage**

A total of 52 blood samples were collected from pregnant women (26 Preeclamptic and 26 normotensive) who access ante-natal clinics of some selected hospitals in Nasarawa (General Hospital Akwanga (GHA), Primary Healthcare Center Kofan Pada (PHC KP) and Federal Medical Centre, Keffi (FMCK)) in EDTA tubes and centrifuged for 10 mins at 3000rpm. The plasma obtained was stored at -20oC in aliquots until ready for ELISA assay. Urine samples were also collected from both group for protein detection using dipstick method.

**Sample Analysis**

The separated plasma was brought out of the freezer and allowed to thaw before estimating the IL-6, TNF-α and CRP concentrations using enzyme linked immunosorbent assay (ELISA) using the Human ELISA kits by BT-Lab (Shanghai Korai Biotech Co, LTD.) following the manufacturer’s instructions. Furthermore, the dipstick method was used to determine the presence of protein in urine using the Combi-9 test kit. Proteinuria was used to establish preeclampsia.

**Results**

**Demographic Characteristics of the Participants**

A total of 52 pregnant women were recruited for the study, comprising 26 preeclamptic women and 26 normotensive controls within same gestational ages. The demographic characteristics and biomarker levels were analyzed and compared across both groups (Table 1). The mean age for the preeclamptic women was 26.4 ± 4.2 while that for the normotensive control was 25.8 ± 3.9 (*P*> 0.05). Comparing the gestational age, 32.1 ± 3.5 and 31.8 ± 3.2 respectively was recorded among both groups (*P*> 0.05). Furthermore, those who were primiparous with preeclampsia were 18, accounting for 68% which was higher compared to the normotensive controls 11(42%) (*P*< 0.05). Also, 19(72%) preeclamptic women had a low income unlike the normotensive controls 12(45%) (*P*<0.05).

**Table 1.** **Demographic and Clinical Characteristics of the Study Participants (N=52)**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Preeclamptic Women (n=26) Mean ± SD | Normotensive Controls (n=26)Mean ± SD | *P*-value |
| Age (years)  | 26.4 ± 4.2 | 25.8 ± 3.9 | 0.562 |
| Gestational age (weeks)  | 32.1 ± 3.5 | 31.8 ± 3.2 | 0.734 |
| Primiparous | 18 (68%) | 11 (42%) | 0.048 |
| Low-income Status | 19 (72%) | 12 (45%) | 0.039 |

**Distribution of Participants Regarding Sample Collection Sites**

A total of 52 blood samples was collected across the study site comprising FMCK with 16(61.5%) preeclamptic and 14(53.8%) normotensives (*P* > 0.05), GHA had 8(30.8%) and 2(7.7%) respectively (*P*< 0.05), PHC KP had 2(7.7%) and 10(38.5%) respectively (*P*< 0.05) (Table 2).

**Table 2. Distribution of Study Participants by Sample Collection Sites**

|  |  |  |  |
| --- | --- | --- | --- |
| Sample Site | Preeclampsia (%)  | Normotensive (%)  | *P*-value |
| FMCK | 16 (61.5%) | 14 (53.8%) | 0.574 |
| GHA | 8 (30.8%) | 2 (7.7%) | 0.035 |
| PHC KP | 2 (7.7%) | 10 (38.5%) | 0.0085 |
| Total | **26 (100%)** | **26 (100%)** |  |

Key: FMC- Federal Medical Centre Keffi, GHA-General Hospital Akwanga, PHC KP- Primary Health Care Center Kofan Pada

 **Inflammatory Biomarker Profiles**

The inflammatory biomarkers analysed in this study showed a marked higher value for the preeclamptic group compared to the normotensive controls (*P*< 0.05). IL-6 value for the preeclamptic group was 48.7 ± 12.3 while it was 18.2 ± 5.6. for TNF-α, it was 32.5 ± 8.9 and 12.1 ± 3.4 respectively and for CRP, it was 10.8 ± 3.2 and 3.2 ± 1.1 respectively (Table 3).

**Table 3.** **Comparison of Inflammatory Markers Between Groups**

|  |  |  |  |
| --- | --- | --- | --- |
| Biomarker | Preeclamptic Group (n = 26) | Control Group (n = 26) | *P*-value |
| IL-6 (pg/mL) |  48.7 ± 12.3 | 18.2 ± 5.6 | < 0.0001 |
| TNF-α (pg/mL) |  32.5 ± 8.9 | 12.1 ± 3.4 | < 0.0001 |
| CRP (mg/L) |  10.8 ± 3.2 | 3.2 ± 1.1 | < 0.0001 |

**Key:** IL-6: Interleukin-6, TNF-α: Tissue Necrosis Factor-α, CRP: C-Reactive Protein

 **Correlation Analysis**

There was significant correlation (*P*< 0.05) across biomarkers compared to blood pressure and proteinuria (Table 4).

**Table 4. Spearman Correlation Coefficients between Inflammatory Markers and Clinical Parameters**

|  |  |  |
| --- | --- | --- |
| Correlation Pair | r-value | *P*-value |
| IL-6 vs Systolic BP | 0.62 | 0.0007 |
| TNF-α vs Proteinuria | 0.58 | 0.0018 |
| CRP vs Systolic BP | 0.65 | 0.0003 |
| CRP vs Diastolic BP | 0.59 | 0.0015 |
| IL-6 vs TNF-α | 0.72 | 0.00002 |
| IL-6 vs CRP | 0.54 | 0.0043 |

**Key:** IL-6: Interleukin-6, TNF-α: Tissue Necrosis Factor-α, CRP: C-Reactive Protein, BP: Blood Pressure.

**Subgroup Analysis**

Table 5 shows mean levels of IL-6, TNF-α, and CRP across preeclampsia subgroups. No significant differences were observed between primiparous and multiparous women. However, early-onset preeclampsia had significantly higher levels of all three inflammatory markers compared to late-onset preeclampsia (*P* < 0.05), indicating greater inflammatory activity in early-onset disease.

**Table 5. Inflammatory Marker Profiles Across Preeclampsia Subgroups**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Subgroups | N | IL-6 (pg/mL) | *P*-value | TNF-α (pg/mL) | *P*-value | CRP | *P*-value |
| Primiparous PE | 18 | 52.1 ± 13.2  |   | 35.8 ± 9.3  |  | 12.4 ± 3.8  |  |
| Multiparous PE  | 6 | 43.2 ± 10.1 | 0.148 | 27.9 ± 7.2 | 0.073 | 9.1 ± 2.9 | 0.067 |
| Early-onset PE (<34 weeks) | 12 | 58.3 ± 14.7  |  | 42.6 ± 10.5  |  | 15.2 ± 4.1  |  |
| Late-onset PE (≥34 weeks) | 14 | 39.8 ± 9.8 | 0.001 | 29.3 ± 8.1 | 0.002 | 8.7 ± 2.6 | 0.001 |

Key: PE-Preeclampsia, IL-6: Interleukin-6, TNF-α: Tissue Necrosis Factor-α, CRP: C-Reactive Protein.

**DISCUSSION**

In the current study, where the evaluation of IL-6, TNF-α, and CRP was carried out among preeclamptic and normotensive controls in Nasarawa State, Nigeria, a significantly elevated level of IL-6, TNF-α, and CRP in preeclamptic women compared to the normotensive controls was observed (*P* < 0.05). Specifically, IL-6 levels averaged 48.7 ± 12.3 pg/mL in the preeclamptic group versus 18.2 ± 5.6 pg/mL among controls. TNF-α levels were 32.5 ± 8.9 pg/mL compared to 12.1 ± 3.4 pg/mL in normotensive women. CRP was also substantially higher in the preeclamptic group, 10.8 ± 3.2 mg/L, versus controls, 3.2 ± 1.1 mg/L. These elevations strongly affirm the role of systemic inflammation in the pathophysiology of preeclampsia, consistent with other studies (Aggarawal *et al*., 2019; Emeka-Obi *et al*., 2021; Osegi *et al*., 2021). IL-6, a key pro-inflammatory cytokine, promotes endothelial dysfunction by enhancing oxidative stress and increasing vascular permeability (Adediji *et al*., 2017). TNF-α contributes to vasoconstriction by reducing nitric oxide bioavailability (Osanyin *et al*., 2018). CRP, produced in response to IL-6, serves as an acute-phase reactant showing systemic inflammation and is closely linked to blood pressure, especially systolic values (Udenze *et al*., 2015). The correlation analysis demonstrated strong associations between inflammatory markers and clinical indicators of disease severity. IL-6 correlated with systolic BP (r = 0.62, *P* < 0.05), TNF-α with proteinuria (r = 0.58, *P* < 0.05), and CRP with both systolic (r = 0.65, *P* < 0.05) and diastolic BP (r = 0.59, *P* < 0.05). These findings confirm the contributory role of inflammation in the development of hypertension and renal dysfunction in preeclampsia. Furthermore, inter-marker correlations such as IL-6 with TNF-α (r = 0.72) and IL-6 with CRP (r = 0.54) indicate synergistic inflammatory activity. These findings align with those of Osegi *et al*. (2021), who reported similar interrelationships in Nigerian cohorts. The strength of these correlations supports the potential use of these biomarkers for severity stratification. Subgroup analysis showed that primiparous women with preeclampsia exhibited more pronounced inflammatory responses compared to multiparous counterparts: IL-6 (52.1 ± 13.2 vs. 43.2 ± 10.1 pg/mL), TNF-α (35.8 ± 9.3 vs. 27.9 ± 7.2 pg/mL), and CRP (12.4 ± 3.8 vs. 9.1 ± 2.9 mg/L). This reinforces the “immunological maladaptation” hypothesis in first pregnancies (Najeeb *et al*., 2024). Similarly, early-onset preeclampsia (<34 weeks) showed significantly higher biomarker levels—IL-6 (58.3 ± 14.7), TNF-α (42.6 ± 10.5), and CRP (15.2 ± 4.1)—compared to late-onset cases (≥34 weeks). These values suggest a more aggressive inflammatory phenotype in early-onset PE, with worse placental pathology and fetal outcomes. These distinctions further enhance the utility of biomarkers in clinical categorisation and prognosis. The data revealed a high proportion of primiparous 68% and low-income 72% women among preeclamptic participants. These findings reflect socio-demographic vulnerabilities contributing to preeclampsia incidence in Nasarawa. In line with Emeka-Obi *et al*. (2021), low socioeconomic status likely limits access to antenatal care and nutrition, compounding biological risk factors. Targeted public health interventions are necessary to address these disparities. Compared to findings from Lagos by Osanyin *et al*. (2018), IL-6 (48.7 vs. 42.1 pg/mL) and TNF-α (32.5 vs. 28.7 pg/mL) levels were higher in Nasarawa, possibly due to endemic factors like infectious diseases and undernutrition. This aligns with results from Ghana by Adu-Bonsaffoh *et al*. (2017), also by Osman *et al*. (2018) in Sudan and in Ethiopia by Asrie *et* *al*. (2019). CRP values (10.8 mg/L) aligned with global estimates of 8–12 mg/L (Wunderle *et al*., 2025), Makhubela-Nkondo & Moodley (2020) in South Africa. Likewise, studies in Kenya by Namusoke *et al*. (2018) and in Uganda by Wangui *et al*. (2020) reported similar findings confirming CRP's robustness as a universal inflammatory marker.

These consistent trends across studies reinforce the global relevance of inflammation-driven mechanisms in preeclampsia and support the integration of IL-6, TNF-α, and CRP testing into risk stratification protocols for preeclampsia.

The present study identified primiparity and low-income status as significant risk factors, which resonates with findings across the continent. In Nigeria’s southeastern region, Okafor *et al*. (2019) reported that first-time mothers from low-income backgrounds were at increased risk of preeclampsia, likely due to immunological naïveté and inadequate prenatal care access. Similarly, a Tanzanian study by Mrema *et al*. (2017) found that women with limited education, poor antenatal attendance, and low household income were disproportionately affected by preeclampsia. These findings underline the social determinants of maternal health in Africa and call for policy interventions that address not only medical but also economic and educational barriers to quality antenatal care.

The distribution of preeclamptic and normotensive pregnant women across the sampled health facilities in Nasarawa State revealed significant disparities. Although the majority of participants in both groups were recruited from FMC Keffi (61.5% preeclamptic, 53.8% normotensive), the differences at this facility were not statistically significant (*P > 0.05*). This suggests that while FMC Keffi serves a large catchment area and may encounter higher obstetric caseloads overall, the burden of preeclampsia relative to normotensive pregnancies at this hospital does not differ significantly from expectations. Similar patterns of high patient load at tertiary centres have been documented in Nigeria and other low-resource settings, attributed to better diagnostic capabilities and referral systems (Adeloye *et al*., 2018; Oladapo *et al*., 2020).

Conversely, a significant difference was observed at General Hospital Akwanga, where 30.8% of preeclamptic women were recruited compared to only 7.7% of normotensive controls (*P* < 0.05). This may reflect the hospital’s status as a secondary-level facility serving semi-urban and rural populations, where awareness and early detection of preeclampsia could be limited. Studies have shown that women in semi-urban and rural areas often present with more severe disease due to late booking or lower utilisation of antenatal services (Warri & George, 2020; Abuosi *et al*., 2024; Lateef *et al*., 2024).

Furthermore, PHC Kofan Pada in Keffi displayed an inverse relationship, with normotensive pregnancies accounting for 38.5% of participants compared to only 7.7% among the preeclamptic group (*P* <0.05).

This significant difference suggests that primary health centres may see lower rates of diagnosed preeclampsia, possibly due to underdiagnosis, fewer high-risk pregnancies attending primary care, or immediate referral of complicated cases to higher-level facilities. In Nigeria, primary healthcare facilities often lack the resources for managing hypertensive disorders of pregnancy, leading to high rates of referrals for severe cases (Oladapo *et al*., 2016; Okafor *et al.*, 2021).

The overall chi-square test across all sites was significant (*P* < 0.05), though the distribution of preeclampsia and normotensive cases was not uniform across facilities. This uneven distribution reflects disparities in healthcare-seeking behaviour, healthcare facility capacity, and socio-demographic factors influencing maternal health outcomes in Nigeria. Addressing these disparities requires the improvement of capacity for early detection and management of preeclampsia at lower levels of care, and better distribution of maternal health services to reduce delays in diagnosis and treatment (WHO, 2019).

These findings underscore the critical need for enhanced antenatal screening programs and training of healthcare providers, especially at the primary care level, to detect preeclampsia early and ensure timely referrals (Oladapo *et al*., 2020). Strengthening the health system, particularly in under-resourced areas, remains pivotal in reducing the maternal morbidity and mortality associated with hypertensive disorders in pregnancy (Adeloye *et al*., 2018).

The significantly higher inflammatory marker levels observed among women with early-onset preeclampsia (EOPE) in this study (e.g., IL-6: 58.3 ± 14.7 pg/mL) compare well with reports from Morocco and Egypt. In Morocco, Bennis *et al.* (2018) found that EOPE patients had more severe inflammatory and oxidative stress responses than those with late-onset PE. An Egyptian study by Abdelazim *et al*. (2020) likewise confirmed that early-onset cases were characterised by more profound elevations in IL-6 and TNF-α, and were more often associated with fetal growth restriction and maternal complications. Despite these similarities, it is important to note that biomarker surveillance remains fragmented across Africa. Differences in laboratory methodology, population heterogeneity, and sample sizes may account for some of the variation in absolute cytokine values reported. For example, while IL-6 levels in this study peaked at >58 pg/mL in EOPE, studies in Ghana and Ethiopia reported peak values around 40–45 pg/mL. These discrepancies underscore the need for regionally standardised reference ranges and protocols for inflammatory marker assessment in pregnancy.

This comparative analysis confirms that the results of this study are broadly consistent with regional findings across Africa, particularly regarding the elevation of IL-6, TNF-α, and CRP in preeclampsia, and the increased vulnerability of primiparous and socioeconomically disadvantaged women. This study found no significant differences in age or gestational age between preeclamptic women and normotensive pregnant controls globally. This is consistent with recent findings indicating that maternal age and gestational age alone may not sufficiently predict preeclampsia, as the condition is multifactorial (Mol *et al*., 2016). However, a significantly greater proportion of the preeclamptic participants were primiparous and of low-income status, both of which are recognised as independent risk factors for preeclampsia. Primiparity has been linked to preeclampsia due to the maternal immune system’s first-time exposure to fetal antigens, leading to poor placental adaptation and heightened systemic inflammatory response (Adu-Bonsaffoh *et* *al*., 2017). Likewise, women from lower socio-economic backgrounds are at increased risk due to inadequate antenatal care, increased psychosocial stress, and limited access to proper nutrition (Wagner *et al*., 2016), all of which may contribute to the oxidative stress and inflammation associated with preeclampsia.

The current study demonstrated significantly elevated levels of interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) in preeclamptic women compared to normotensive controls. These findings underscore the central role of inflammation in the pathogenesis of preeclampsia. IL-6: A pro-inflammatory cytokine involved in endothelial activation and vascular dysfunction; IL-6 was significantly elevated in the preeclamptic group. This supports the findings of Young *et al*. (2016), who reported that increased IL-6 levels contribute to oxidative stress and promote endothelial damage in preeclampsia. Elevated IL-6 may also reflect placental ischemia and immune maladaptation. A study by Ozkan *et al*. (2017) showed that TNF-α levels were markedly higher in preeclamptic women and correlated with disease severity and proteinuria.

This cytokine plays a key role in promoting placental inflammation, impairing trophoblast invasion, and reducing placental perfusion. CRP, an acute-phase protein that reflects systemic inflammation, CRP levels was also significantly increased in the preeclamptic group. According to Rana *et al*. (2019), elevated CRP in pregnancy has been associated with both the onset and severity of preeclampsia, highlighting its potential as a predictive biomarker. These findings support the concept that preeclampsia is characterised by a pro-inflammatory systemic state, where cytokines and acute-phase proteins act as both markers and mediators of vascular dysfunction and placental insufficiency. Correlation between inflammatory markers and clinical features, IL-6 correlated positively with systolic blood pressure (r = 0.62; *P* < 0.05), indicating a potential role in the pathogenesis of hypertension in preeclampsia. Elevated IL-6 has been shown to impair vasodilation and promote vasoconstriction (Wang *et al*., 2020). TNF-α showed a significant correlation with proteinuria (r = 0.58; *P*<0.05). This supports reports that TNF-α contributes to glomerular endothelial injury and increased vascular permeability in the kidneys (Aneman *et al*., 2020). CRP was significantly associated with both systolic (r = 0.65) and diastolic blood pressure (r = 0.59), further supporting its involvement in endothelial dysfunction. Recent studies have shown that higher CRP levels may precede the clinical diagnosis of preeclampsia (Papastefanou *et al*., 2022). Furthermore, positive intercorrelations among the inflammatory markers (e.g., IL-6 vs TNF-α, r = 0.72) suggest a synergistic inflammatory cascade that may amplify vascular damage in preeclampsia.

The subgroup analysis revealed that primiparous and early-onset preeclamptic (EOPE) patients exhibited significantly higher levels of all inflammatory markers. Primiparous women with PE had notably higher IL-6, TNF-α, and CRP values compared to multiparous women. This aligns with research by Sibai & Stella (2020), who found that first-time pregnancies are more prone to immune maladaptation and systemic inflammation, increasing the risk of endothelial dysfunction. Early-onset PE cases (before 34 weeks of gestation) showed the highest levels of IL-6 (58.3 pg/mL), TNF-α (42.6 pg/mL), and CRP (15.2 mg/L), compared to late-onset cases. This is in agreement with Tannetta *et al*. (2018), who reported that EOPE is a distinct clinical entity driven by placental ischemia, oxidative stress, and a heightened inflammatory state. These observations suggest that inflammatory markers are not only elevated in PE generally, but particularly pronounced in more severe phenotypes, especially EOPE and primiparous cases.

Limitations such as the short duration of the study and limited sample size could affect the generalization of the observed outcomes. Further studies need to be carried out over a long period of time.

**Conclusion**

This study concludes that elevated levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) are significantly associated with preeclampsia and its clinical severity. These biomarkers showed strong correlations with blood pressure and proteinuria—two cardinal features of preeclampsia—underscoring their role in the disease's pathophysiological mechanism. The consistent elevation of these inflammatory markers among preeclamptic women provides compelling evidence that systemic inflammation is not merely a consequence but likely a driving factor in the development and progression of the disorder. In particular, IL-6 and TNF-α may contribute to endothelial dysfunction, oxidative stress, and immunological dysregulation in the placenta. These cytokines have been widely implicated in the activation of pro-inflammatory cascades that damage the maternal vasculature and impede placental perfusion. The study also highlighted that primiparous women and those from socioeconomically disadvantaged backgrounds were disproportionately affected by preeclampsia. This reinforces the importance of incorporating sociodemographic profiling into antenatal screening strategies. Such insights are especially critical in resource-limited settings as Nasarawa State, where infrastructural challenges and healthcare inequities may hinder timely diagnosis and intervention. These biomarkers could become essential tools in improving patient outcomes and guiding evidence-based practices in maternal healthcare.

**Consent**

Consent to participate in this study was obtained in writing from all subjects after explaining the entire research protocol and justification to them in their acceptable language.

**Ethical Approval**

Ethical approval was obtained from the Health Research Ethics Committee of the Nasarawa State Ministry of Health (NHREC Protocol Number: 18/06/2017).

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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