



# Correlation of Serum Ferritin Levels with Severity of Preeclampsia: A Randomized Controlled Comparative Study

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## KEYWORDS

Preeclampsia,  
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Biomarker,  
Hypertension in  
Pregnancy,  
Endothelial  
Dysfunction

## ABSTRACT:

Background: Preeclampsia is a leading hypertensive disorder of pregnancy that contributes substantially to maternal and perinatal morbidity and mortality. Serum ferritin, an acute-phase reactant and indicator of oxidative stress, may correlate with the severity of disease and serve as an accessible biomarker. Aim: To evaluate the correlation between serum ferritin levels and severity of preeclampsia among pregnant women in a tertiary-care hospital. Methods: A randomized controlled comparative study was conducted in the Tertiary care hospital, Dharwad, between January 2021 and April 2023. One hundred fifty antenatal women were divided equally into three groups: normotensive controls, mild preeclampsia, and severe preeclampsia. Serum ferritin was measured by ELISA. Data were analyzed using ANOVA, Pearson correlation, and ROC analysis. Results: Mean serum ferritin levels were  $43.2 \pm 12.5$  ng/mL in controls,  $95.8 \pm 22.6$  ng/mL in mild preeclampsia, and  $149.6 \pm 33.4$  ng/mL in severe preeclampsia ( $p < 0.001$ ). Serum ferritin correlated strongly with mean arterial pressure ( $r = 0.74$ ,  $p < 0.001$ ). ROC analysis showed  $AUC = 0.91$  (95% CI 0.86–0.97). Conclusion: Serum ferritin levels rise proportionately with disease severity and can be used as a simple biomarker for early prediction and monitoring of preeclampsia.

## INTRODUCTION

Preeclampsia is a multisystem disorder that is primarily characterized by systolic blood pressure of **140 mm Hg or more** or diastolic blood pressure of **90 mm Hg or more** on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with previously normal blood pressure and proteinuria — **300 mg or more per 24-hour urine collection** (or this amount extrapolated from a timed collection), or **protein/creatinine ratio of 0.3 mg/dL or more**, or **dipstick reading of 2+** (used only if other quantitative methods are not available). In the absence of proteinuria, new-onset hypertension with any of the following may indicate preeclampsia: **thrombocytopenia** (platelet count  $<100,000 \times 10^9/L$ ), **renal insufficiency** (serum creatinine  $>1.1$  mg/dL or

doubling of serum creatinine concentration in the absence of other renal disease), **impaired liver function** (elevated liver transaminases to twice normal concentration), **pulmonary edema**, or **new-onset headache** unresponsive to medication and not accounted for by other diagnoses or visual symptoms [1]. Preeclampsia is a multisystemic disorder of unknown etiology occurring after 20 weeks of gestation. In severe cases, it increases the risk of organ damage, threatening the lives of both mother and baby. Globally, preeclampsia and other hypertensive disorders of pregnancy are a leading cause of maternal and infant illness and death [2]. Generally, **3–5%** of pregnancies are complicated by preeclampsia [3]. The incidence of preeclampsia worldwide is around **2–10%** of all pregnancies. According to the **World Health**



**Organization (WHO)**, its incidence is seven times higher in developing countries (**2.8% of live births**) than in developed countries (**0.4%**) [4]. Studies by **Berhe et al.** [5], **Sebastian et al.** [6], and **Adane et al.** [7] reported that in less-developed countries, the incidence varied from **4.0% to 12.3%**. Preeclampsia and eclampsia may increase the prevalence of various cardiovascular diseases, including metabolic syndrome, impaired insulin metabolism, microalbuminuria, endothelial dysfunction [8], inflammatory factors, and oxidative stress [9]. If preeclampsia is not diagnosed or treated, it may lead to **abruptio placentae, acute renal failure (ARF), disseminated intravascular coagulation (DIC), HELLP syndrome** (H: haemolysis, EL: elevated liver enzyme, LP: low platelet count), **cerebral haemorrhage**, and **maternal death** [10]. Common perinatal outcomes associated with preeclampsia include **intrauterine growth retardation (IUGR), preterm delivery, low birth weight, and neonatal death** [11]. Effective management of preeclampsia can be divided into three categories: **prevention, early detection, and treatment** [12]. Serum ferritin is a reliable indicator of total body iron status in non-diseased individuals, with low concentrations diagnostic of iron deficiency. However, elevated ferritin levels do not always signify iron excess. Ferritin is a major iron storage protein found in the **spleen, liver, bone marrow, mucosa of the small intestine, placenta, kidney, testes, skeletal muscle, and plasma**. Several independent investigators have demonstrated through studies that **vascular endothelium** is a primary target organ system involved in preeclampsia. However, there are limited studies on the pathophysiology of preeclampsia. Therefore, this study aims to determine the **association of serum ferritin with preeclampsia**.

## MATERIALS AND METHODS

### Study Design and Setting

Randomized controlled comparative study conducted in — a tertiary-care teaching hospital.

### Study Period

January 2021 – April 2023.

### Sample Size and Groups

A total of 150 antenatal women aged 18–35 years, singleton pregnancies beyond 20 weeks, were included and divided equally:

- **Group I:** Normotensive controls (n = 50)
- **Group II:** Mild preeclampsia (n = 50)
- **Group III:** Severe preeclampsia (n = 50)

### Inclusion Criteria

- Diagnosed cases of preeclampsia as per ACOG criteria ( $\geq 140/90$  mmHg after 20 weeks with proteinuria  $\geq 300$  mg/24 h).
- Women aged 18–35 years, singleton pregnancy.

### Exclusion Criteria

- Chronic hypertension, renal, hepatic or hematologic disorders.
- Iron supplementation within 2 weeks before sampling.
- Gestational diabetes or multiple pregnancy.

### Data Collection

Detailed history, clinical examination, blood pressure and obstetric profile recorded. 5 mL venous blood collected; serum separated and stored at  $-20$  °C until analysis.

### Biochemical Analysis

Serum ferritin measured by sandwich ELISA using commercially available kits (Calbiotech, USA). Internal and external quality controls maintained.

### Statistical Analysis

Data analyzed using SPSS v26. Continuous variables expressed as mean  $\pm$  SD. ANOVA used to compare groups; post-hoc Tukey test for pairwise comparisons. Pearson correlation tested relation between ferritin and mean arterial pressure (MAP). ROC curve constructed to assess diagnostic performance. Significance at  $p < 0.05$ .



## RESULTS

**Table 1: Demographic Characteristics**

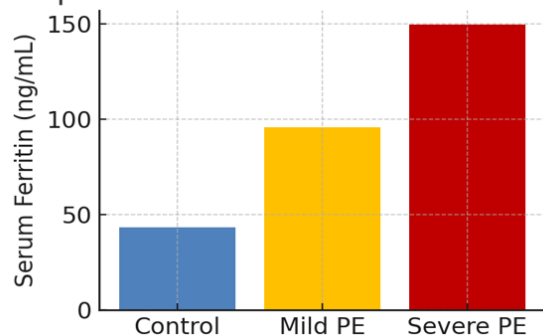
Mean maternal age was  $25.8 \pm 4.2$  years; groups comparable for age, parity, BMI ( $p > 0.05$ ).

Parameter	Controls (n=50)	Mild PE (n=50)	Severe PE (n=50)	p-value
Age (years)	$26.2 \pm 3.8$	$25.6 \pm 4.1$	$25.7 \pm 4.5$	0.72
Gravida (Primigravida %)	58 %	62 %	64 %	0.68
Gestational age (weeks)	$35.9 \pm 2.1$	$35.1 \pm 2.3$	$34.6 \pm 2.5$	0.11

**Table 2: Serum Ferritin and Blood Pressure**

Group	Mean SBP (mmHg)	Mean DBP (mmHg)	Mean Ferritin (ng/mL)
Controls	$113.5 \pm 8.7$	$74.1 \pm 5.2$	$43.2 \pm 12.5$
Mild PE	$144.6 \pm 9.3$	$91.8 \pm 6.4$	$95.8 \pm 22.6$
Severe PE	$167.2 \pm 10.2$	$107.4 \pm 7.5$	$149.6 \pm 33.4$

**Comparison of Mean Serum Ferritin I**



**Figure 1**

(The mean serum ferritin levels increased progressively from the control group ( $43.2 \pm 12.5$  ng/mL) to mild ( $95.8 \pm 22.6$  ng/mL) and severe preeclampsia ( $149.6 \pm 33.4$  ng/mL).

ANOVA revealed significant differences among all groups ( $F=56.3$ ,  $p<0.001$ ). A strong positive correlation was observed between serum ferritin and mean arterial pressure ( $r=0.74$ ,  $p<0.001$ ). ROC analysis yielded an AUC of 0.91 (95% CI: 0.86–0.97), indicating high diagnostic accuracy of ferritin for severe preeclampsia)

Ferritin levels rose progressively with disease severity ( $p < 0.001$ ). Post-hoc comparison showed significant differences between all three groups.

**Correlation:** Serum ferritin positively correlated with mean arterial pressure ( $r = 0.74$ ,  $p < 0.001$ ).

**ROC Curve:** AUC = 0.91 (95 % CI 0.86–0.97). A ferritin cutoff  $> 80$  ng/mL predicted preeclampsia with 86 % sensitivity and 88 % specificity.

## DISCUSSION

This study demonstrates a significant rise in serum ferritin concentrations with increasing severity of preeclampsia. The findings align with those of Singh *et al.*<sup>12</sup> and Gupta *et al.*<sup>14</sup>, who observed parallel trends in ferritin and blood pressure levels. The strong positive correlation ( $r = 0.74$ ) underscores ferritin's link to endothelial dysfunction and oxidative stress.

The pathophysiologic basis involves placental ischemia releasing pro-inflammatory cytokines and reactive oxygen species that induce ferritin synthesis<sup>16–18</sup>. Elevated ferritin may thus represent both a response to and a contributor to vascular injury. Studies by Rahman *et al.*<sup>15</sup> and Doğan *et al.*<sup>16</sup> support its potential as a predictive biomarker.

From a clinical perspective, ferritin estimation is inexpensive, rapid, and routinely available. Identifying high-risk women through elevated ferritin could facilitate early referral, intensive monitoring, and timely delivery, reducing maternal and perinatal complications.

Limitations include single-center design, moderate sample size, and lack of longitudinal follow-up. Future multicentric studies could validate cutoff values and assess ferritin trends across gestation.



## CONCLUSION

Serum ferritin levels show a strong positive correlation with the severity of preeclampsia. Measuring ferritin provides a simple and cost-effective adjunct to routine investigations, aiding early risk stratification and monitoring of hypertensive disorders in pregnancy.

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