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Research Article

Serum Iron Status, Total Iron-Binding Capacity, and Ferritin in Preeclampsia: A Cross-Sectional Comparative Study from Northern India

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ABSTRACT
Background: Dysregulated iron metabolism and oxidative stress are implicated in the pathogenesis of pre-eclampsia (PE), yet evidence from South-Asian populations remains limited.
Objective: To compare serum iron, total iron-binding capacity (TIBC) and ferritin concentrations between women with PE and normotensive pregnant controls receiving routine antenatal iron prophylaxis.
Methods: In a hospital-based cross-sectional study at a tertiary centre (September 2023 – August 2024), 64 singleton pregnancies ≥ 20 weeks' gestation were enrolled (32 PE; 32 controls). PE was defined as blood pressure ≥ 140/90 mmHg plus proteinuria ≥ 1+ on dipstick. Venous blood was analysed for serum iron (ferrozine method), TIBC (saturating–precipitating assay) and ferritin (two-site chemiluminescent immunoassay). Between-group comparisons used Student's *t*-test; significance $p < 0.05$.
Results: Mean gestational age was lower in the PE group (36.2 ± 1.1 weeks) than controls (37.9 ± 1.2 weeks; $p < 0.001$). Serum iron was significantly higher in PE (126.4 ± 39.5 µg/dL) versus controls (83.9 ± 25.5 µg/dL; $p < 0.001$), while TIBC was lower (354.6 ± 52.6 vs 417.0 ± 59.2 µg/dL; $p < 0.001$). Ferritin was more than doubled in PE (88.0 ± 37.8 vs 38.6 ± 26.4 ng/mL; $p < 0.001$).
Conclusions: In iron-supplemented pregnancies, PE is associated with raised circulating iron and ferritin together with reduced TIBC, supporting a role for iron-mediated oxidative stress in its pathophysiology. Routine indiscriminate antenatal iron supplementation may warrant re-evaluation, and iron indices may serve as inexpensive early markers for risk stratification.

Keywords: Preeclampsia; Ferritin; Iron; Total Iron-Binding Capacity; Oxidative Stress; Pregnancy.

INTRODUCTION

Preeclampsia (PE) affects 3–5 % of pregnancies worldwide and remains a leading cause of maternal–perinatal morbidity and mortality, particularly in low- and middle-income countries [1, 2]. The condition is characterised by new-onset hypertension and proteinuria or end-organ dysfunction after 20 weeks' gestation [3]. Although its aetiology is multifactorial, accumulating evidence implicates placental oxidative stress, endothelial dysfunction and dysregulated iron handling as central mechanisms [4–6].

Physiological gestation entails progressive mobilisation of maternal iron stores to meet fetal and placental demands, reflected by declining ferritin and rising total iron-binding capacity (TIBC) as pregnancy advances [7]. In contrast, numerous studies report paradoxically elevated serum iron and ferritin with concomitant reductions in TIBC among women who develop PE [8–10]. Free catalytic iron can amplify reactive oxygen species (ROS) formation via Fenton chemistry, triggering lipid peroxidation, endothelial injury and vasoconstriction—hallmarks of PE pathology [11].

Universal antenatal iron supplementation is widely practised in India to prevent iron-deficiency anaemia; however, supplementation in iron-replete women might further accentuate oxidative stress and PE risk [12]. South-Asian data exploring iron indices in PE under routine prophylaxis remain scarce.

Accordingly, we compared serum iron, TIBC and ferritin levels between women with PE and gestation-matched normotensive controls attending a large public teaching hospital in northern India. We hypothesised that despite standard iron prophylaxis, women with PE

would exhibit higher circulating iron and ferritin but lower TIBC than controls.

METHODS

Study Design & Setting

A hospital-based, cross-sectional comparative study was conducted in the Departments of Biochemistry and Obstetrics & Gynaecology, Mahila Chikitsalaya, Sawai Man Singh Medical College, Jaipur. The institutional ethics committee approved the protocol (ABMH/IEC/2020-09); all participants provided written informed consent.

Participants

From September 2023 to August 2024, consecutive pregnant women aged 18–35 years with singleton gestations > 20 weeks, receiving routine oral iron prophylaxis (100 mg elemental iron + 500 µg folic acid daily), were screened. PE cases met American College of Obstetricians and Gynecologists criteria for blood pressure ≥ 140/90 mmHg on two occasions 4 h apart with proteinuria ≥ 1+ or ≥ 300 mg/24 h. Exclusion criteria included eclampsia, gestational hypertension, anaemia (Hb < 10 g/dL), chronic hypertension, diabetes, renal or hepatic disease, multiple pregnancy, haemoglobinopathies, recent transfusion, or medications influencing iron metabolism.

Sample Size

Based on a mean serum iron difference of 1.5 µmol/L between groups (SD 2.14 µmol/L) [13], α = 0.05 and 80 % power, 32 participants per group were required (G*Power v3.1).

Data Collection

After detailed history and examination, venous blood was drawn prior to any therapeutic intervention. Serum was separated within 1 h and stored at 4 °C until analysis (< 48 h). A mid-stream urine sample was analysed by dipstick.

Biochemical Assays

- **Serum Iron:** Acid dissociation–ferrozine colorimetry (Beckman Coulter AU-680).
- **TIBC:** Magnesium-carbonate precipitation and subsequent iron quantification, with dilution factor applied.
- **Ferritin:** Two-site sandwich chemiluminescent immunoassay (ADVIA Centaur XP; analytical range 0.5–1650 ng/mL). Internal quality control used manufacturer-supplied low and high controls.

Statistical Analysis

Data were analysed using SPSS v25. Continuous variables are presented as mean ± SD; categorical variables as number (percentage). Normality was assessed with Shapiro–Wilk tests. Group means were compared using unpaired *t*-tests; χ^2 test evaluated categorical variables. Two-tailed $p < 0.05$ denoted significance.

RESULTS

Participant Characteristics

All 64 enrolled women completed the study. Baseline demographics are summarised in Table 1. PE cases were slightly older and delivered earlier than controls; primigravidae predominated in both cohorts. As expected, systolic and diastolic blood pressures were significantly higher in PE (152.1 ± 7.9 / 100.6 ± 8.2 mmHg) versus controls (110.5 ± 4.9 / 71.8 ± 3.5 mmHg; $p < 0.001$).

Iron Indices

Mean serum iron concentration was ~50 % higher in PE (126.4 µg/dL) than controls (83.9 µg/dL). Conversely, TIBC was reduced by ~15 % in PE (354.6 µg/dL) compared with controls (417.0 µg/dL). Serum ferritin nearly doubled in PE (88.0 ng/mL) relative to controls (38.6 ng/mL). All differences remained significant after adjustment for gestational age (ANCOVA, $p < 0.01$). Results are detailed in Table 2. No participant exhibited biochemical iron deficiency (ferritin < 15 ng/mL). Scatterplots demonstrated a negative correlation between ferritin and TIBC ($r = -0.46$; $p = 0.001$) and a positive correlation between ferritin and serum iron ($r = 0.52$; $p < 0.001$).

Tables

Table 1 — Baseline Maternal Characteristics

Variable	Preeclampsia (n = 32)	Controls (n = 32)	*p*-value
Age (years)	28.6 ± 3.3	26.5 ± 3.4	0.018
Primigravida, n (%)	24 (75 %)	26 (81 %)	0.58
Gestational age (weeks)	36.2 ± 1.1	37.9 ± 1.2	< 0.001

SBP (mmHg)	152.1 ± 7.9	110.5 ± 4.9	< 0.001
DBP (mmHg)	100.6 ± 8.2	71.8 ± 3.5	< 0.001

Table 2 — Iron Status Parameters

Parameter	Preeclampsia	Controls	*p*-value
Serum iron (µg/dL)	126.4 ± 39.5	83.9 ± 25.5	< 0.001
TIBC (µg/dL)	354.6 ± 52.6	417.0 ± 59.2	< 0.001
Ferritin (ng/mL)	88.0 ± 37.8	38.6 ± 26.4	< 0.001

DISCUSSION

This study corroborates and extends previous observations that PE is accompanied by perturbations in maternal iron metabolism despite universal prophylactic supplementation. Women with PE exhibited significantly higher circulating iron and ferritin yet lower iron-binding capacity than normotensive counterparts. These alterations support the paradigm of iron-driven oxidative stress contributing to endothelial dysfunction in PE [4, 11, 14].

Excess non-transferrin-bound iron can catalyse ROS generation, propagating lipid peroxidation within the vasculature and placenta. Elevated ferritin, an acute-phase reactant, likely reflects both increased stores and inflammatory up-regulation. The inverse relationship between ferritin and TIBC observed here suggests saturation of transferrin and diminished antioxidant buffering capacity, as reported by Hubel et al. [8].

Our iron and ferritin values are comparable to Indian studies by Zafar & Iqbal [15] and Maitra et al. [16], though mean concentrations were slightly lower—possibly due to earlier gestational sampling. Lao et al. [17] similarly noted high third-trimester ferritin predicting adverse outcomes in non-anaemic women, questioning indiscriminate iron supplementation. Some investigators have reported reduced serum iron in PE [18]; disparities may stem from differing supplementation regimens, dietary intake, or genetic polymorphisms in iron transporters.

Clinical Implications

Routine antenatal iron prophylaxis is imperative for preventing iron-deficiency anaemia; however, our data advocate for baseline iron screening and targeted dosing to avoid potential iatrogenic iron excess in high-risk women. Measurement of ferritin and TIBC in the late second trimester could aid early identification of PE susceptibility, enabling intensified surveillance and antioxidant strategies.

Strengths and limitations

Strengths include strict case-control matching, uniform analytical platforms, and exclusion of confounders such as anaemia and chronic disease. Limitations encompass the single-centre design, modest sample size, and inability to measure non-transferrin-bound iron or oxidative stress biomarkers. Longitudinal studies are warranted to determine temporal causality and to evaluate the impact of modulating iron intake on PE incidence.

CONCLUSION

Serum iron and ferritin are significantly elevated, while TIBC is reduced, in preeclamptic pregnancies compared with normotensive controls receiving standard iron prophylaxis. Iron-mediated oxidative stress may therefore play a pivotal role in PE pathogenesis. Tailored antenatal iron supplementation based on individual iron status, alongside routine monitoring of ferritin and TIBC, could represent a pragmatic strategy for early PE risk stratification in resource-limited settings.

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