ORIGINAL ARTICLE

A prospective cohort study of serum iron profile values estimated during early pregnancy and their correlation with hypertensive disorders of pregnancy

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Abstract

Background: Hypertensive Disorders of Pregnancy (HDP) are among the leading causes of maternal and perinatal morbidity and mortality worldwide. Alterations in maternal iron metabolism and inflammatory markers during early pregnancy have been proposed to contribute to the pathogenesis of HDP. *Aim and Objectives:* To evaluate the association between maternal serum iron profile parameters measured in early pregnancy and the development of HDP and to assess their relationship with maternal and neonatal outcomes. *Material and Methods:* This prospective cohort study was conducted at a tertiary care hospital from March 2024 to December 2025. Singleton pregnant women aged 18-35 years with gestation between 12 and 19+6 weeks were enrolled (Out of 100 enrolled, 95 were assessed for outcomes). Serum iron, ferritin, Total Iron-Binding Capacity (TIBC), and transferrin saturation were estimated at recruitment. Participants were followed and assessed for the development of HDP, gestational age at delivery, maternal and neonatal outcomes. *Results:* Among 95 participants, 14.7% developed hypertensive disorders of pregnancy. Serum iron and transferrin saturation did not show significant associations with HDP or maternal and neonatal outcomes. TIBC showed a significant association only with mode of delivery. In contrast, serum ferritin was significantly higher among women who developed HDP and among those with adverse maternal and neonatal outcomes, including preterm birth, low birth weight, and NICU admission. *Conclusion:* Serum iron, transferrin saturation, and TIBC showed no significant association with HDP or outcomes, whereas elevated serum ferritin was significantly associated with HDP and adverse maternal and neonatal outcomes indicating its potential role as an acute phase inflammatory marker and risk indicator in early pregnancy for subsequent development of HDP.

Keywords: Pregnancy complications; Iron metabolism; Oxidative stress; Placental insufficiency

Introduction

Hypertension and anemia are among the most common medical complications of pregnancy and remain as major contributors to maternal and perinatal morbidity and mortality [1]. Hypertensive Disorders of Pregnancy (HDP), which include Gestational Hypertension (GHTN) and Pre-Eclampsia (PE), affect approximately 5–10% of pregnant women and are associated with significant adverse maternal and fetal outcomes [2]. PE is characterized by hypertension with proteinuria or evidence of end-organ dysfunction [3]. PE is a multisystem disorder originating at the maternal –fetal interface and is frequently complicated by renal, hepatic, neurological, hematological, and cardiovascular dysfunction, as well as Fetal Growth Restriction (FGR), stillbirth, and maternal death [4-6]. Oxidative stress is a key mechanism causing pregnancy-induced hypertension. Abnormal trophoblastic invasion and incomplete spiral artery remodeling in early pregnancy result in placental hypoxia leading to endothelial dysfunction and vasoconstriction [3].

Iron dysregulation may aggravate this process: iron overload enhances Reactive Oxygen Species (ROS) generation, while iron deficiency contributes to mitochondrial dysfunction and oxidative injury. Both extremes can disrupt placental development, impair vascular reactivity, and predispose to hypertension and PE [3]. Few research have demonstrated that lower serum iron levels in women later developed HDP, others showing higher iron levels in PE, and several reporting no significant association [3,4]. Micronutrients are necessary for proper development during pregnancy, and iron plays a central role in oxygen transport, cellular metabolism, and oxidative balance [7-9]. Iron deficiency is highly prevalent in pregnancy and is linked to anemia, impaired immunity, preterm delivery, and Low Birth Weight (LBW) [9]. Conversely, excessive iron levels and high hemoglobin concentrations following supplementation showed links to adverse effects, including an increased risk of HDP suggesting that both deficiency and excess of iron may be harmful during gestation, highlighting the importance of balanced iron homeostasis [9].

Given these conflicting reports and the biological plausibility further evaluation of maternal iron status in relation to HDP is warranted. Therefore, the present study aimed to assess the association of maternal iron profile parameters measured in early pregnancy with the development of HDP and with maternal and neonatal outcomes.

Materials and Methods

This prospective observational study was conducted from March 2024 to December 2025 in the Department of Obstetrics and Gynecology at a tertiary care hospital after obtaining approval from the Institutional Ethics Committee (IEC No: BLDE (DU)/IEC-SBMPMC/114/2023-24).

Pregnant women attending the antenatal clinic were screened for eligibility. Singleton pregnant women aged 18 to 35 years with a gestational age of ≥ 12 weeks and < 19 weeks + 6 days were included in the study. Women with chronic hypertension, conditions known to influence iron metabolism or serum ferritin levels, such as chronic infections, malignancy, renal, hepatic or cardiac diseases, haemochromatosis, recent history of blood transfusion or parenteral iron therapy within the preceding three months, and known haemoglobinopathies, were excluded. Pregnancies complicated by fetal congenital anomalies and prior history of anemia with hemoglobin levels below 11 g/dL were also excluded.

Sample size was calculated based on findings by Ahmed *et al.* (2023) [10], which showed a mean serum ferritin level of 29.3 ± 5.075 ng/mL. With a confidence level of 99% and a margin of error of 1.5, using the formula $n = (Z \times \sigma / d)^2$, where $Z = 2.05$, $\sigma = 5.075$ and $d = 1.5$, minimum required sample size was 48 participants.

Clinical history and complete general and obstetric examination were performed at recruitment. Baseline demographic data and clinical parameters were recorded using a structured proforma. Venous blood samples were taken during routine antenatal visits for estimation of iron profile parameters. All participants received routine antenatal care and prophylactic oral iron supplementation as per national guidelines. They were followed up regularly during subsequent antenatal visits and monitored for HDP. Maternal and neonatal outcomes were documented at the time of delivery.

The interpretation of iron profile parameters was based on standard reference intervals for women of reproductive age (16-40 years) as per reference ranges described in standard texts Bishop *et al*. (2010) [11]. The normal reference range for serum

iron was taken as 45–150 µg/dL, for serum ferritin as 10-120 ng/mL, for transferrin as 200-380 mg/dL, for transferrin saturation as 15-50%, and for TIBC as 250-425 µg/dL. Values below or above these ranges were categorized as low or high, respectively, for analytical purposes.

Data were entered in Microsoft Excel and analysis was done using Statistical Package for the Social Sciences software version 26. Continuous variables were showed as mean ± Standard Deviation (SD) and analyzed using independent t-test or one way ANOVA. Categorical variables were showed as frequencies and percentages and analyzed using Chi-square test. A value of $p < 0.05$ was considered statistically significant.

Results

In this study 320 pregnant women were screened, out of which 220 pregnant women were excluded (n = 120 not willing for follow up, n = 58 had mild to moderate anemia before enrolment, n = 42 had prior history of anemia correction). Most participants were aged 18–25 years (76.8%), with mean of 23.49 ± 3.27 years. The majority resided in urban areas (73.7%). Multigravida women constituted 67.4%, while 32.6% were primigravida. Nearly half had parity of one (47.4%). A history of abortion was absent in 89.5% of cases. The mean maternal weight was 57.07 ± 6.74 kg. Mean pulse rate was 82.51 ± 5.89/min, systolic blood pressure 114.19 ± 8.91 mmHg, and diastolic blood pressure 75.64 ± 6.99 mmHg (Table 1).

Serum iron and transferrin saturation showed comparable distributions between women with and without HDP, with no statistically significant differences ($p > 0.05$). Mean serum iron levels were 43.8 ± 15.5 µg/dL in the non-HDP group and 41.3 ± 16.7 µg/dL in the HDP group. Serum ferritin differed significantly between groups ($p = 0.043$), with higher mean ferritin levels in the HDP group (95.9 ± 14.7 ng/mL) compared to the non-HDP group (59.3 ± 10.8 ng/mL). TIBC and transferrin saturation did not show significant associations with HDP (Table 2).

Mean serum iron and transferrin saturation values were similar across normotensive women and HDP subgroups, with no significant differences ($p > 0.05$). Serum ferritin showed a significant increasing trend across groups ($p = 0.041$), with the highest mean levels observed in PE with severe features (115.4 ± 3.5 ng/mL) compared to normotensive women (59.3 ± 10.8 ng/mL). TIBC also differed significantly among groups ($p = 0.008$), with higher mean values in PE without severe features (556.8 ± 57.8 µg/dL) and PE with severe features (548.0 ± 53.7 µg/dL) than in normotensive women (464.2 ± 64.1 µg/dL) (Table 3).

Serum iron, TIBC, and transferrin saturation showed no significant associations with maternal outcomes, mode of delivery, gestational age at birth, birth weight, or Neonatal Intensive Care Unit (NICU) admission (all $p > 0.05$). In contrast, serum ferritin demonstrated significant associations with adverse maternal and neonatal outcomes, including maternal complications ($p = 0.038$), mode of delivery ($p = 0.041$), preterm birth ($p = 0.042$), LBW ($p = 0.040$), and NICU admission ($p = 0.037$). Higher ferritin levels were consistently observed among women with complications, preterm deliveries, LBW infants, and neonates requiring NICU admission (Tables 4 & 5).

Table 1: Distribution of study participant according to maternal characteristic

Variable		N (%)	Mean ± S.D.
Age n (%)	**18-25 years**	73 (76.8%)	23.49 + 3.268
	26-35 years	22 (23.2%)	
Residence	**Urban**	70 (73.7%)	-
	Rural	25 (26.3%)	-
Gravida	**Primigravida**	31 (32.6)	-
	Multigravida	64 (67.4)	-
Weight		-	57.07 + 6.739
Gestational age at recruitment (weeks)		-	15.994 + 2.637
Pulse Rate		-	82.51 + 5.885
Systolic Blood Pressure			114.19 + 8.906
Diastolic Blood Pressure		-	75.64 + 6.996

Table 2: Association of iron profile with HDP among study participants

Iron profile parameter (Normal range)	Category	No HDP n (%)	HDP n (%)	*p*
Serum Iron (45–150 µg/dL)	**Low**	21 (25.9)	3 (21.4)	0.616
	Normal	59 (72.8)	10 (71.4)	
	High	1 (1.2)	1 (7.1)	
	Mean ± SD	43.8 ± 15.5	41.3 ± 16.7	
Serum Ferritin (10–120 ng/mL)	**Low**	6 (7.4)	1 (7.1)	0.043
	Normal	33 (40.7)	6 (42.9)	
	High	42 (51.9)	7 (50.0)	
	Mean ± SD	59.3 ± 10.8	95.9 ± 14.7	
TIBC (250–425 µg/dL)	**Low**	5 (6.2)	3 (21.4)	0.362
	Normal	46 (56.8)	10 (71.4)	
	High	30 (37.0)	1 (7.1)	
	Mean ± SD	464.2 ± 64.1	518.1 ± 63.9	

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Transferrin Saturation (15–50%)	**Low**	7 (8.6)	1 (7.1)	0.491
	Normal	47 (58.0)	12 (85.7)	
	High	27 (33.3)	1 (7.1)	
	Mean ± SD	32.7 ± 7.9	33.6 ± 8.7	

HDP – hypertensive disorders of pregnancy; TIBC – total iron binding capacity; SD – standard deviation

Table 3: Association of iron profile with HDP study participants

Parameter	Group	Mean ± SD	Low n (%)	Normal n (%)	High n (%)	*p*
Serum Iron (µg/dL)	**Normotensive (n = 81)**	43.8 ± 15.5	21 (25.9)	59 (72.8)	1 (1.2)	0.5891
	GHTN (n = 7)	46.2 ± 15.5	1 (14.3)	5 (71.4)	1 (14.3)	
	PE without severe features (n = 5)	34.5 ± 16.0	1 (20.0)	4 (80.0)	0 (0.0)	
	PE with severe features (n = 2)	41.4 ± 19.0	1 (50.0)	1 (50.0)	0 (0.0)	
Serum Ferritin (ng/mL)	**Normotensive (n = 81)**	59.3 ± 10.8	6 (7.4)	33 (40.7)	42 (51.9)	0.041
	GHTN (n = 7)	81.4 ± 8.3	0 (0.0)	3 (42.9)	4 (57.1)	
	PE without severe features (n = 5)	101.2 ± 6.7	1 (20.0)	2 (40.0)	2 (40.0)	
	PE with severe features (n = 2)	115.4 ± 3.5	0 (0.0)	1 (50.0)	1 (50.0)	
TIBC (µg/dL)	**Normotensive (n = 81)**	464.2 ± 64.1	5 (6.2)	46 (56.8)	30 (37.0)	0.008*
	GHTN (n = 7)	473.9 ± 76.3	2 (28.6)	5 (71.4)	0 (0.0)	
	PE without severe features (n = 5)	556.8 ± 57.8	1 (20.0)	3 (60.0)	1 (20.0)	
	PE with severe features (n = 2)	548.0 ± 53.7	0 (0.0)	2 (100.0)	0 (0.0)	

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Transferrin Saturation (%)	**Normotensive (n = 81)**	32.7 ± 7.9	7 (8.6)	47 (58.0)	27 (33.3)	0.2864
	GHTN (n = 7)	30.9 ± 10.6	1 (14.3)	5 (71.4)	1 (14.3)	
	PE without severe features (n = 5)	39.2 ± 7.6	0 (0.0)	5 (100.0)	0 (0.0)	
	PE with severe features (n = 2)	29.6 ± 7.3	0 (0.0)	2 (100.0)	0 (0.0)	

** Statistically significant*

HDP – hypertensive disorders of pregnancy; PE – pre-eclampsia; GHTN – gestational hypertension; TIBC – total iron binding capacity; SD – standard deviation

Table 4: Iron profile and maternal and neonatal outcomes

Outcome	Group (n)	Low n (%)	Normal n (%)	High n (%)	Mean ± SD	*p*
Serum Iron (45-150 µg/dL)						
Maternal outcome	**APH (9)**	2 (22.2)	6 (66.7)	1 (11.1)	88.6 ± 19.8	0.622
	PPH (7)	1 (14.3)	5 (71.4)	1 (14.3)	89.4 ± 17.4	
	No complication (79)	20 (25.3)	58 (73.4)	1 (1.3)	90.6 ± 18.9	
Mode of delivery	**LSCS (45)**	12 (26.7)	32 (71.1)	1 (2.2)	89.6 ± 19.4	0.619
	Vaginal (50)	12 (24.0)	37 (74.0)	1 (2.0)	92.1 ± 18.0	
Gestational age	**Preterm (13)**	2 (15.4)	10 (76.9)	1 (7.7)	88.7 ± 19.9	0.627
	Term (82)	22 (26.8)	59 (72.0)	1 (1.2)	92.1 ± 18.3	
Birth weight	**LBW (18)**	7 (38.9)	10 (55.6)	1 (5.6)	88.9 ± 20.1	0.621
	Normal (77)	17 (22.1)	59 (76.6)	1 (1.3)	92.6 ± 18.0	
NICU admission	**Yes (10)**	1 (10.0)	9 (90.0)	0 (0.0)	87.9 ± 20.6	0.629
	No (85)	23 (27.1)	60 (70.6)	2 (2.4)	92.8 ± 18.1	

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Serum Ferritin (10-120 ng/mL)						
Maternal outcome	**APH (9)**	2 (22.2)	2 (22.2)	5 (55.6)	87.3 ± 32.1	0.038*
	PPH (7)	1 (14.3)	2 (28.6)	4 (57.1)	84.1 ± 29.3	
	No complication (79)	7 (8.9)	29 (36.7)	43 (54.4)	55.2 ± 24.9	
Mode of delivery	**LSCS (45)**	2 (4.4)	21 (46.7)	22 (48.9)	58.9 ± 15.1	0.041*
	Vaginal (50)	5 (10.0)	18 (36.0)	27 (54.0)	50.6 ± 13.4	
Gestational age	**Preterm (13)**	1 (7.7)	4 (30.8)	8 (61.5)	80.6 ± 33.9	0.042*
	Term (82)	6 (7.3)	35 (42.7)	41 (50.0)	54.9 ± 25.7	
Birth weight	**LBW (18)**	3 (16.7)	4 (22.2)	11 (61.1)	82.7 ± 34.8	0.040*
	Normal (77)	4 (5.2)	35 (45.5)	38 (49.4)	53.8 ± 24.6	
NICU admission	**Yes (10)**	1 (10.0)	4 (40.0)	5 (50.0)	85.4 ± 36.7	0.037*
	No (85)	6 (7.1)	35 (41.2)	44 (51.8)	53.1 ± 23.9	

** Statistically significant*

APH – antepartum haemorrhage; PPH – postpartum haemorrhage; LBW – low birth weight; LSCS – lower segment caesarean section; NICU – neonatal intensive care unit; TIBC – total iron binding capacity

Table 5: Serum Profile and Maternal and Neonatal Outcomes

TIBC (250–425 µg/dL)						
Maternal outcome	**APH (9)**	2 (22.2)	6 (66.7)	1 (11.1)	340.2 ± 43.1	0.371
	PPH (7)	1 (14.3)	5 (71.4)	1 (14.3)	339.6 ± 46.5	
	No complication (79)	6 (7.6)	47 (59.5)	26 (32.9)	331.7 ± 43.6	
Mode of delivery	**LSCS (45)**	7 (15.6)	28 (62.2)	10 (22.2)	336.4 ± 45.8	0.359
	Vaginal (50)	1 (2.0)	28 (56.0)	21 (42.0)	328.6 ± 41.9	
Gestational age	**Preterm (13)**	0 (0.0)	8 (61.5)	5 (38.5)	338.6 ± 45.7	0.366
	Term (82)	8 (9.8)	48 (58.5)	26 (31.7)	330.8 ± 43.2	

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Birth weight	**LBW (18)**	1 (5.6)	13 (72.2)	4 (22.2)	337.6 ± 46.8	0.368
	Normal (77)	7 (9.1)	43 (55.8)	27 (35.1)	328.9 ± 42.4	
NICU admission	**Yes (10)**	0 (0.0)	6 (60.0)	4 (40.0)	339.6 ± 49.3	0.372
	No (85)	8 (9.4)	50 (58.8)	27 (31.8)	327.4 ± 41.6	
Transferrin Saturation (15–50%)						
Maternal outcome	**APH (9)**	1 (11.1)	7 (77.8)	1 (11.1)	25.5 ± 7.5	0.495
	PPH (7)	1 (14.3)	5 (71.4)	1 (14.3)	26.1 ± 6.9	
	No complication (79)	7 (8.9)	48 (60.8)	24 (30.4)	27.5 ± 6.3	
Mode of delivery	**LSCS (45)**	6 (13.3)	27 (60.0)	12 (26.7)	26.3 ± 6.8	0.487
	Vaginal (50)	2 (4.0)	32 (64.0)	16 (32.0)	27.6 ± 6.1	
Gestational age	**Preterm (13)**	3 (23.1)	7 (53.8)	3 (23.1)	26.3 ± 6.9	0.493
	Term (82)	5 (6.1)	52 (63.4)	25 (30.5)	27.6 ± 6.2	
Birth weight	**LBW (18)**	1 (5.6)	11 (61.1)	6 (33.3)	25.8 ± 7.2	0.496
	Normal (77)	7 (9.1)	48 (62.3)	22 (28.6)	27.8 ± 6.0	
NICU admission	**Yes (10)**	0 (0.0)	4 (40.0)	6 (60.0)	25.2 ± 7.4	0.498
	No (85)	8 (9.4)	55 (64.7)	22 (25.9)	27.9 ± 6.0	

** Statistically significant*

APH – antepartum haemorrhage; PPH – postpartum haemorrhage; LBW – low birth weight; LSCS – lower segment caesarean section; NICU – neonatal intensive care unit; TIBC – total iron binding capacity

Discussion

The maternal baseline profile in the present study showed a predominance of young women, with most participants belonging to 18 to 25 years age group and a mean age of 23.49 years, which is comparable to antenatal cohorts reported by Ahmed *et al*. (2023) and Wang *et al*. (2023) [10,12]. The higher proportion of multigravida women and largely normotensive blood pressure values at recruitment indicate that the cohort represents routine antenatal attendees. Similar distributions of age, parity, and baseline blood pressure in earlier studies support the external validity of this sample and permit meaningful comparison of iron profile parameters with existing literature [12,13].

Serum iron levels did not show a significant association with HDP or with any outcomes in the present study. Ahmed *et al*. (2023) and Wang *et al*.

(2023) also reported no significant differences between normotensive and hypertensive pregnant women [10,12]. This suggests that circulating serum iron alone may not adequately reflect the underlying pathophysiological alterations in HDP and has limited value as an isolated predictive marker for adverse outcomes.

In contrast, serum ferritin demonstrated a significant association with HDP and few outcomes in the present study, including preterm birth, LBW, and NICU admission. Higher ferritin levels were observed among women with HDP and those with unfavorable outcomes. Similarly, other reports by earlier investigators described elevated ferritin levels in PE and attributed this to inflammatory activation rather than iron status alone [13,14]. Previous studies linking raised ferritin with fetal growth retardation and LBW, such as those by Akkurt *et al*. (2017) are also supported by the present observations [15]. The results strengthen the evidence that serum ferritin, as an acute-phase reactant and marker of iron storage, may reflect placental dysfunction and systemic inflammation associated with HDP.

TIBC showed no consistent association with HDP or any outcomes. Although a statistically significant difference was observed with respect to mode of delivery. Ahmed *et al*. (2023) also observed both comparable or reduced TIBC values in PE, suggesting that TIBC is relatively preserved and less sensitive to disease severity [10]. Overall, these results indicate that TIBC has limited independent predictive value for HDP or related neonatal outcomes.

Transferrin saturation showed no significant associations with HDP or any outcomes. Ahmed *et al*. (2023) and Wang *et al*. (2023) also found minimal variation in transferrin saturation between hypertensive and normotensive pregnancies [10,12]. The absence of strong associations suggests that iron transport and immediate availability remain relatively stable, while alterations in iron storage and inflammatory markers, particularly ferritin, appear to be more closely related to the pathological processes underlying hypertensive disorders of pregnancy.

Conclusion

Early pregnancy iron profile parameters showed differential associations with HDP and maternal –neonatal outcomes. Serum iron, transferrin saturation, and TIBC did not demonstrate consistent or clinically meaningful relationships with HDP or adverse outcomes. In contrast, serum ferritin was significantly higher among women with HDP and those experiencing adverse maternal and neonatal outcomes, suggesting a possible role as a marker of inflammatory activity and placental dysfunction rather than iron status alone. These findings indicate that while most iron profile parameters have limited value as standalone predictors, serum ferritin may have potential utility in identifying pregnancies at risk for hypertensive complications and unfavorable perinatal outcomes.

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