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ORIGINAL RESEARCH ARTICLE

Maternal Serum Ferritin Concentrations in Pregnancies Complicated by Preterm Labour or Preterm Prelabour Rupture of Membranes: A Comparative Observational Study

Manjushree Waikar[1] | Mansi Shrigiriwar[2*] | Snehal Vitthalrao Lede[1] | Ayushi Pashine[1] | Surbhi Agrawal[1]

Abstract

Background: Ferritin reflects both iron stores and acute-phase inflammation. Its concentration may differ in pregnancies complicated by spontaneous preterm labour or preterm prelabour rupture of membranes (PPROM), but contemporaneous measurement after clinical presentation cannot establish prediction.

Objective: To compare maternal serum ferritin concentrations among women with PPROM, spontaneous preterm labour, and uncomplicated pregnancies at 28–36+6 weeks of gestation, and to describe associated maternal laboratory findings and perinatal outcomes.

Methods: This hospital-based comparative observational study enrolled 210 pregnant women at a tertiary centre in Central India from June 2024 to January 2026: 70 with PPROM, 70 with spontaneous preterm labour, and 70 controls. Serum ferritin was measured by immunoturbidimetry. Continuous outcomes were compared using Welch's one-way analysis of variance with Games–Howell pairwise tests; categorical variables were compared using Pearson's chi-square test.

Results: Mean (SD) ferritin was 20.89 (10.10) ng/mL in controls, 59.39 (40.30) ng/mL in PPROM, and 41.23 (25.20) ng/mL in preterm labour (Welch $F(2, 109.01)=45.40$; $p<0.001$). Compared with controls, the mean difference was 38.50 ng/mL for PPROM (95% CI, 26.63–50.37) and 20.34 ng/mL for preterm labour (95% CI, 12.61–28.07); PPROM also exceeded preterm labour by 18.16 ng/mL (95% CI, 4.67–31.65). Leukocyte counts were higher and haemoglobin was lower in both complication groups, whereas C-reactive protein positivity did not differ. Gestational age at sampling and documented vaginitis/urinary tract infection also differed substantially among groups. Infants in the PPROM and preterm-labour groups delivered earlier, weighed less, and were more often admitted to neonatal intensive care.

Conclusions: Maternal ferritin was higher at presentation with PPROM or spontaneous preterm labour than in controls. Because ferritin was measured after diagnosis and the groups differed in gestational age and infection status, these data support ferritin as a concurrent inflammatory correlate, not as a validated independent screening or predictive test. Prospective studies with prespecified sampling, multivariable adjustment, and external validation are required.

Key words: ferritin, preterm labour, preterm prelabour rupture of membranes, inflammation, pregnancy, neonatal outcomes

1 | INTRODUCTION

Preterm birth, defined as birth before 37 completed weeks of gestation, remains a major cause of neonatal mortality and long-term morbidity worldwide. Spontaneous preterm labour and preterm prelabour rupture of membranes (PPROM) are leading pathways to spontaneous

[1]Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Nagpur, Maharashtra, India.

[2]Associate Professor, Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Ayodhya Nagar, Nagpur 440024, Maharashtra, India.

Address correspondence to: Mansi, Shrigiriwar, Associate Professor, Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Ayodhya Nagar, Nagpur 440024, Maharashtra, India, *Email: muktai2008@gmail.com*

preterm birth. Their clinical consequences include respiratory morbidity, neonatal infection, prolonged neonatal intensive care, and neurodevelopmental impairment (1–5).

Inflammatory activation—whether related to infection or sterile intrauterine inflammation—contributes to cervical remodelling, uterine contractility, and weakening of the fetal membranes (3, 4, 6). Ferritin is principally an iron-storage protein, but it also behaves as an acute-phase reactant. In healthy pregnancy, ferritin commonly declines as maternal iron requirements increase; inflammation can instead increase circulating ferritin and complicate its interpretation as a marker of iron status (7).

Prior observational studies have linked higher maternal ferritin with spontaneous preterm birth, preterm labour, and PPROM, although the timing of sampling, definitions of elevated ferritin, and degree of adjustment for inflammation and other confounders vary widely (8–12). A prospective cohort found only modest adjusted associations between early-pregnancy ferritin and subsequent spontaneous preterm birth, underscoring that contemporaneous case–control separation does not itself establish predictive performance (10).

We therefore compared maternal serum ferritin concentrations among women presenting with PPROM, women with spontaneous preterm labour, and pregnant controls without either condition at a tertiary centre in Central India. Secondary objectives were to compare other laboratory indices, selected clinical risk factors, and maternal and neonatal outcomes across groups. We hypothesised that ferritin concentrations would be highest in PPROM, intermediate in spontaneous preterm labour, and lowest in controls.

2 | MATERIALS AND METHODS

2.1 | Study design and setting

This hospital-based comparative observational study was conducted in the outpatient department and labour room of the Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Nagpur, Maharashtra, India, from June 2024 through January 2026. Women were enrolled by convenience sampling and followed through delivery for the reported maternal and neonatal outcomes. Reporting was guided by the STROBE recommendations for observational studies (13).

2.2 | Participants and study groups

The study included 210 pregnant women between 28+0 and 36+6 weeks of gestation, with 70 participants in each of three prespecified clinical groups:

- PPROM: documented clinical diagnosis of rupture of membranes before 37 weeks and before the onset of labour.
- Spontaneous preterm labour: documented regular uterine contractions with cervical change before 37 completed weeks, without PPROM.
- Control: pregnancy at 28+0 to 36+6 weeks without preterm labour or PPROM at enrolment.

Eligible women had a haemoglobin concentration greater than 10.5 g/dL and provided written informed consent. Exclusion criteria were active labour at enrolment, multifetal pregnancy, haemoglobin concentration of 10.5 g/dL or less, known liver disease, diabetes mellitus, pregnancy-induced hypertension or pre-eclampsia, or refusal to participate.

2.3 | Data collection and laboratory measurements

A standardised proforma captured demographic characteristics, obstetric history, clinical risk factors, laboratory indices, delivery information, and neonatal outcomes. After clinical assessment, 2 mL of venous blood was obtained at enrolment. Samples were centrifuged, and serum ferritin was measured by an immunoturbidimetric method on a Beckman Coulter AU480 analyser. Haemoglobin, total leukocyte count, and C-reactive protein (CRP) status were recorded. For descriptive analysis, ferritin was categorised as <30, 30–50, or >50 ng/mL; these categories were not treated as validated diagnostic thresholds.

2.4 | Outcomes

The primary outcome was maternal serum ferritin concentration at enrolment. Secondary laboratory outcomes were haemoglobin, total leukocyte count,

and CRP positivity. Other secondary outcomes were maternal hospital stay, gestational age at delivery, neonatal birth weight, and neonatal intensive care unit (NICU) admission.

2.5 | Statistical analysis

Continuous variables are reported as mean (SD), and categorical variables as number (percentage). Because group variances were unequal for several continuous outcomes, between-group comparisons were reanalysed using Welch's one-way analysis of variance. When the overall ferritin comparison was significant, Games–Howell tests provided multiplicity-adjusted pairwise mean differences and 95% confidence intervals. Categorical variables were compared using Pearson's chi-square test. For visual comparison across differently scaled continuous measures, unadjusted Hedges g values and 95% confidence intervals were calculated from the reported group means, SDs, and sample sizes. All tests were two-sided; $p<0.05$ was considered statistically significant. Analyses were performed using SPSS version 23.0 and independently checked against the reported group summaries.

2.6 | Ethics

The Institutional Ethics Committee and Institutional Review Board of Government Medical College and Hospital, Nagpur, approved the study. All participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki.

3 | RESULTS

3.1 | Participant characteristics

The analysis included 210 women, 70 per group. Maternal age and parity were comparable, whereas gestational age at sampling differed (Welch $F(2, 128.48)=22.11$; $p<0.001$). The PPROM group was sampled at the earliest mean gestational age and the preterm-labour group at the latest (Table 1).

Table 1. Baseline demographic and obstetric characteristics (N=210)

Characteristic	Control(n=70)	PPROM(n=70)	Preterm labour(n=70)	Test statistic	p value
Age, years	24.74 (3.98)	25.86 (3.73)	25.77 (4.44)	Welch F=1.71(df 2,137.33)	0.185
Age group, n (%)				χ^2=8.455(df 6)	0.207
<20 years	6 (8.6)	4 (5.7)	7 (10.0)		
21–25 years	35 (50.0)	27 (38.6)	28 (40.0)		
26–30 years	23 (32.9)	30 (42.9)	20 (28.6)		
>30 years	6 (8.6)	9 (12.9)	15 (21.4)		
Gestational age at sampling, weeks	32.77 (2.69)	31.87 (1.08)	33.12 (1.16)	Welch F=22.11(df 2,128.48)	<0.001
Parity, n (%)				χ^2=4.594(df 6)	0.597
0	19 (27.1)	17 (24.3)	18 (25.7)		
1	23 (32.9)	19 (27.1)	18 (25.7)		
2	17 (24.3)	17 (24.3)	13 (18.6)		
3	11 (15.7)	17 (24.3)	21 (30.0)		

Values are mean (SD) unless otherwise indicated. Percentages are within study group. PPROM, preterm prelabour rupture of membranes; df, degrees of freedom.

3.2 | Ferritin and laboratory indices

Ferritin differed across groups (Welch $F(2, 109.01)=45.40$; $p<0.001$). Games–Howell comparisons showed higher ferritin in PPROM than in controls (mean difference, 38.50 ng/mL; 95% CI, 26.63–50.37; $p<0.001$), higher ferritin in preterm labour than in controls (20.34 ng/mL; 95% CI, 12.61–28.07; $p<0.001$), and higher ferritin in PPROM than in preterm labour (18.16 ng/mL; 95% CI, 4.67–31.65; $p=0.005$). Figure 1 shows the group means and precision, while Figure 2 displays the three adjusted

pairwise effect estimates. Haemoglobin and total leukocyte count also differed across groups, but CRP positivity did not (Table 2).

Table 2. Serum ferritin and laboratory parameters by study group (N=210)

Parameter	Control(n=70)	PPROM(n=70)	Preterm labour(n=70)	Test statistic	p value
Serum ferritin, ng/mL	20.89 (10.10)	59.39 (40.30)	41.23 (25.20)	Welch F=45.40(df 2,109.01)	<0.001
Haemoglobin, g/dL	11.53 (0.28)	11.14 (0.19)	11.21 (0.24)	Welch F=47.45(df 2,134.47)	<0.001
Leukocyte count, cells/μL	10,399.93 (903.62)	14,171.53 (1,032.54)	13,125.69 (1,173.08)	Welch F=285.67(df 2,136.47)	<0.001
CRP positive, n (%)	37 (52.9)	33 (47.1)	35 (50.0)	χ^2=0.457(df 2)	0.796

Values are mean (SD) unless otherwise indicated. CRP, C-reactive protein; PPROM, preterm prelabour rupture of membranes.

3.3 | Ferritin categories

Ferritin category was strongly associated with study group (χ^2 (4)=249.018; p<0.001). All controls had ferritin <30 ng/mL. Within the PPROM group, 77.1% had ferritin >50 ng/mL; within the preterm-labour group, 72.9% had ferritin of 30–50 ng/mL (Table 3). These post-presentation categories describe separation among the enrolled clinical groups and do not establish screening thresholds.

Table 3. Ferritin category by study group (N=210)

Ferritin category	Control(n=70)	PPROM(n=70)	Preterm labour(n=70)	Total(N=210)
<30 ng/mL	70 (100.0)	0 (0.0)	8 (11.4)	78 (37.1)
30–50 ng/mL	0 (0.0)	16 (22.9)	51 (72.9)	67 (31.9)
>50 ng/mL	0 (0.0)	54 (77.1)	11 (15.7)	65 (31.0)
Total	70 (100.0)	70 (100.0)	70 (100.0)	210 (100.0)

Values are n (column %). Pearson χ^2=249.018, df=4, p<0.001. PPROM, preterm prelabour rupture of membranes.

3.4 | Clinical risk factors

Documented vaginitis or urinary tract infection differed substantially among groups (χ^2 [2] =72.117; p<0.001): it was present in 68.6% of women with PPROM, 44.3% with preterm labour, and no controls. Previous PPROM, previous preterm labour, and vaginal bleeding in the current pregnancy did not differ significantly (Table 4).

3.5 | Maternal and neonatal outcomes

Maternal hospital stay did not differ significantly. Birth weight and gestational age at delivery were lower in the PPROM and preterm-labour groups, and NICU admission was more common (Table 5). The standardized profile in Figure 3 shows that the largest absolute group differences were in gestational age at delivery, birth weight, and leukocyte count; these unadjusted effects describe separation from controls rather than independent associations. No participant-level analysis was available to determine whether ferritin was independently associated with neonatal outcomes after accounting for gestational age or clinical group.

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Table 4. Selected clinical risk factors by study group (N=210)

Variable	Category	Control(n=70)	PPROM(n=70)	Preterm labour(n=70)	χ^2 (df); p value
Previous PPROM	Yes	33 (47.1)	40 (57.1)	34 (48.6)	1.639 (2); 0.441
	No	37 (52.9)	30 (42.9)	36 (51.4)	
Previous preterm labour	Yes	40 (57.1)	38 (54.3)	31 (44.3)	2.556 (2); 0.279
	No	30 (42.9)	32 (45.7)	39 (55.7)	
Vaginitis/urinary tract infection	Yes	0 (0.0)	48 (68.6)	31 (44.3)	72.117 (2); <0.001
	No	70 (100.0)	22 (31.4)	39 (55.7)	
Vaginal bleeding in current pregnancy	Yes	42 (60.0)	34 (48.6)	37 (52.9)	1.878 (2); 0.391
	No	28 (40.0)	36 (51.4)	33 (47.1)	

Values are n (column %). PPROM, preterm prelabour rupture of membranes.

Table 5. Maternal and neonatal outcomes by study group (N=210)

Outcome	Control(n=70)	PPROM(n=70)	Preterm labour(n=70)	Test statistic	p value
Hospital stay, days	5.54 (2.70)	6.13 (2.77)	5.57 (2.22)	Welch F=1.08(df 2,136.51)	0.344
Birth weight, g	2,917.10 (173.06)	2,068.41 (204.78)	2,172.17 (206.27)	Welch F=437.87(df 2,137.01)	<0.001
Gestational age at delivery, weeks	38.40 (0.90)	32.62 (1.49)	33.60 (1.45)	Welch F=520.76(df 2,129.72)	<0.001
NICU admission, n (%)	0 (0.0)	51 (72.9)	42 (60.0)	χ^2=85.806(df 2)	<0.001

Values are mean (SD) unless otherwise indicated. NICU, neonatal intensive care unit; PPROM, preterm prelabour rupture of membranes

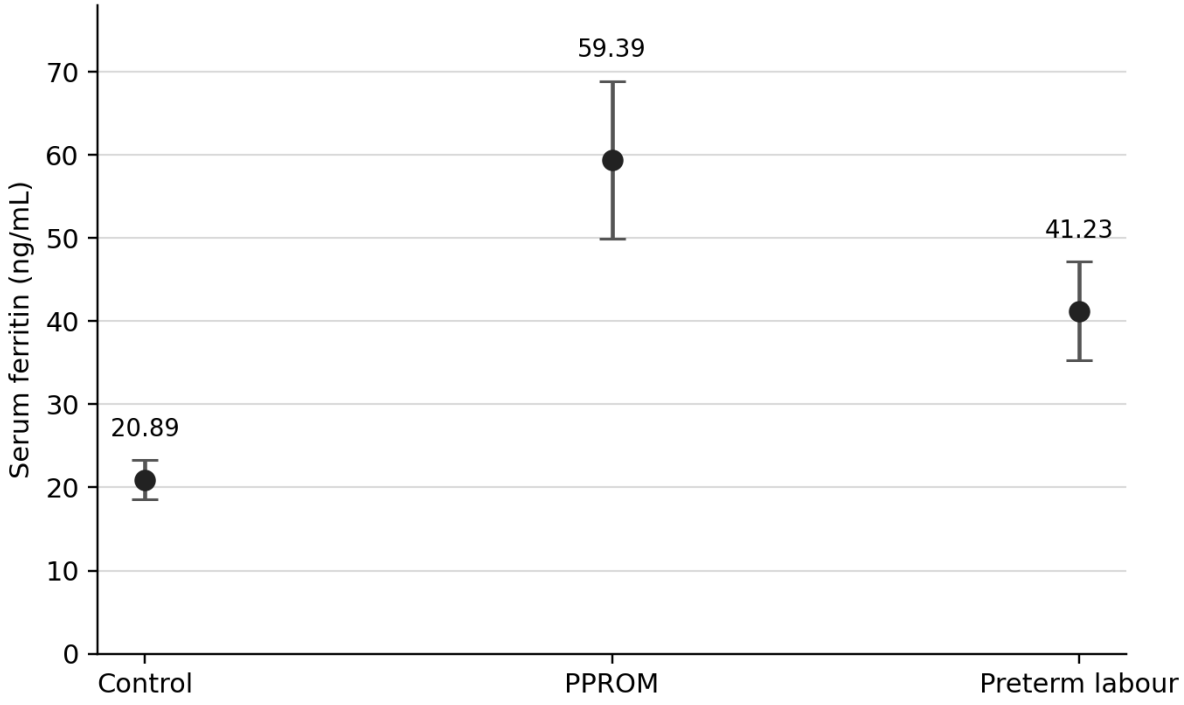

Fig. 1: Mean maternal serum ferritin concentration by study group

Points show group means; error bars show 95% confidence intervals calculated from the reported SD and n=70 per group. PPROM, preterm prelabour rupture of membranes.

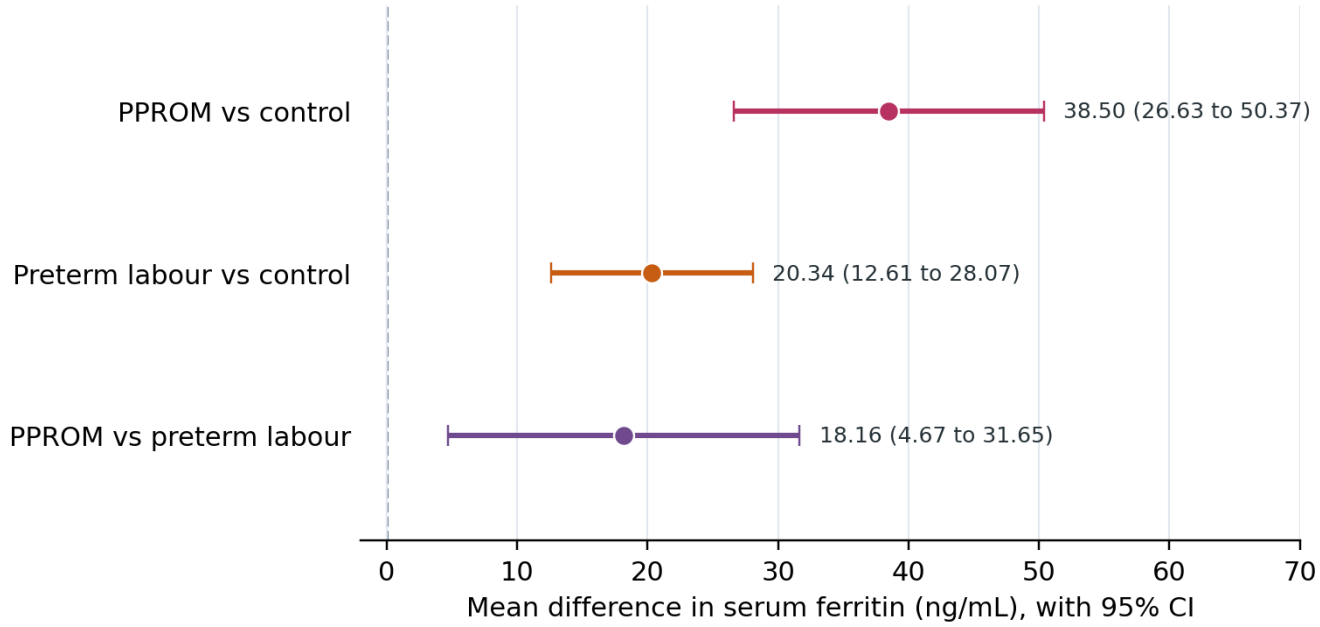

Fig. 2: Pairwise differences in mean serum ferritin concentration

Points and horizontal lines show Games–Howell mean differences and 95% confidence intervals. Positive values indicate higher ferritin in the first-named group. PPROM, preterm prelabour rupture of membranes.

Points and horizontal lines show unadjusted Hedges g values and 95% confidence intervals calculated from group summaries (n=70 per group). Positive values indicate higher and negative values lower measurements than controls. PPROM, preterm prelabour rupture of membranes.

4 | DISCUSSION

4.1 | Principal findings

Maternal serum ferritin measured at enrolment was substantially higher in women presenting with PPROM or spontaneous preterm labour than in controls. The pattern was graded: PPROM had the highest mean concentration, followed by preterm labour and controls, and each pairwise comparison remained significant after Games–Howell adjustment. Leukocytosis and lower haemoglobin in the complication groups were consistent with systemic or pregnancy-related inflammatory differences, although CRP positivity did not vary across groups.

The categorical analysis produced striking clinical-group separation: all controls had ferritin below 30 ng/mL, while most PPROM participants had values above 50 ng/mL. This should be interpreted cautiously. Ferritin was measured after the clinical diagnosis, the thresholds were descriptive rather than prespecified from a validated model, and no sensitivity, specificity, receiver-operating-characteristic analysis, calibration, or external validation was performed. The present findings therefore demonstrate concurrent association, not screening accuracy or prediction.

Fig. 3: Standardized differences in laboratory and neonatal outcomes relative to controls

4.2 | Comparison with previous evidence

The direction of association is consistent with earlier work. Goldenberg and colleagues reported that higher maternal ferritin preceded early spontaneous preterm delivery (8). Abdel-Malek and colleagues identified higher ferritin among women who subsequently delivered preterm and proposed a 31 ng/mL cut-off, although their sampling occurred before outcome ascertainment and their setting differed from ours (9). Khambalia and colleagues, in a cohort of 2,254 women sampled in early pregnancy, reported modest adjusted associations between elevated ferritin and spontaneous preterm birth and emphasised confounding by maternal characteristics and inflammatory conditions (10). Al Bayati and Mohammed observed the highest ferritin in PPROM, intermediate values in spontaneous preterm labour, and the lowest values in controls, closely paralleling the ordering in our study (11). An Indian tertiary-centre study likewise reported higher ferritin in PPROM (12) (13)

These studies collectively support biological plausibility but also show why ferritin is difficult to interpret. Ferritin integrates iron stores, hepatic regulation, and inflammatory signalling. In pregnancy, gestational age, iron supplementation, anaemia, infection, metabolic disease, and maternal adiposity may alter its concentration (7, 10). A single universal threshold is therefore unlikely to perform consistently across populations or sampling windows.

4.3 | Clinical interpretation

Ferritin may be a useful adjunct when interpreted alongside symptoms, examination, gestational age, blood counts, and other inflammatory measures. It should not be used as a stand-alone test to diagnose PPROM or preterm labour on the basis of these data. Importantly, ferritin was obtained after presentation; thus, the study cannot show that measuring ferritin earlier would identify women before symptoms or improve maternal or neonatal outcomes.

The poorer neonatal outcomes in the PPROM and preterm-labour groups were expected because these groups delivered substantially earlier than controls. The available aggregate data do not establish that ferritin independently explains birth weight or NICU

admission. Such a claim would require participant-level regression or mediation analyses that account for gestational age at delivery, infection, clinical group, treatment, and other prognostic factors.

4.4 | Strengths and limitations

Strengths include balanced group sizes, a single laboratory platform, inclusion of two major spontaneous-preterm-birth phenotypes, and reassessment with methods robust to unequal variances. The study also reports clinically relevant delivery and neonatal outcomes.

Several limitations are important. First, convenience sampling at one tertiary centre limits generalisability and may introduce selection bias. Second, ferritin was measured after PPROM or preterm-labour presentation, precluding temporal or predictive inference. Third, gestational age at sampling and documented vaginitis/urinary tract infection differed markedly across groups; either could confound the ferritin comparison. Fourth, only a binary CRP result was available, and data on iron supplementation, body mass index, smoking, socioeconomic status, microbiology, liver indices, and other inflammatory markers were not reported. Fifth, the analysis lacked participant-level multivariable adjustment, diagnostic-accuracy evaluation, missing-data reporting, and an externally validated threshold. Finally, the neonatal comparisons were unadjusted for gestational age at delivery and clinical management.

5 | CONCLUSION

Maternal serum ferritin concentrations were higher at clinical presentation in women with PPROM and spontaneous preterm labour than in pregnant controls, with the highest concentrations in PPROM. These findings support ferritin as a concurrent correlate of the inflammatory and clinical state. They do not establish ferritin as an independent screening, diagnostic, or prognostic biomarker. A prospective multicentre cohort with ferritin measured before symptoms, prespecified thresholds, participant-level multivariable modelling, and external validation is needed before clinical implementation.

6 | DECLARATIONS

Ethics approval and consent to participate: The Institutional Ethics Committee and Institutional Review Board of Government Medical College and Hospital, Nagpur, approved the study. Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

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Competing interests: The authors declare no competing interests.

Data availability: The data underlying this study are available from the corresponding author on reasonable request, subject to institutional and ethical requirements.

Author contributions: All authors contributed to the study conception or design, data acquisition or interpretation, critical revision of the manuscript, and approval of the final version, and agree to be accountable for the work.

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