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ROLE OF CORD FERRITIN IN PREDICTING IRON STORES IN TERM VS LATE PRETERM NEONATES - A CROSS-SECTIONAL STUDY

Dr. Abirami R[1], Dr. Arunkumar T[2], Dr. Ashok C[3]

[1]M.D. Pediatrics Junior resident, Department of Paediatrics, SRM Medical college hospital and research centre, Kattankulathur.abiramiraju65@gmail.com
[2]MBBS, MD (Paediatrics), Assistant Professor, Department of Paediatrics, SRM Medical college hospital and research centre, Kattankulathur.
[3]Professor, Department of Paediatrics, SRM Medical college hospital and research centre, Kattankulathur.

ABSTRACT

INTRODUCTION

Fetal iron accretion occurs mostly during the third trimester of pregnancy; therefore, late preterm infants (34 to 36 weeks) are at greater risk than term infants of being born with depleted iron reserves. Serum ferritin concentration in umbilical cord blood is a valid, non-invasive marker of neonatal iron reserves and correlates with fetal iron status at birth.

AIM: The purpose of the study was to examine role of cord blood ferritin in predicting iron stores at term vs late preterm neonates between 34weeks – 36weeks.

METHODOLOGY: A hospital based analytical cross-sectional study was undertaken in the Department of Paediatrics, SRM Medical College Hospital and Research Centre, Tamil Nadu from May 2025 to January 2026. A total of 96 neonates (48 term, 48 late preterm) born between 34+0 and 41+6 weeks of gestation were enrolled after informed maternal agreement was obtained. Exclusion criteria included neonates with sepsis, congenital malformations, cyanotic heart disease, Rh isoimmunization, and substantial maternal diseases. The umbilical cord venous blood was obtained soon after birth for serum ferritin determination by chemiluminescent immunoassay.

RESULTS: Maternal parameters (age, parity, iron supplementation, hemoglobin, method of birth and obstetric problems) were equivalent in both groups ($P>0.05$). Late preterm neonates had a significantly different birth weight distribution and higher NICU admissions (22.9% vs. 4.2%, $P=0.007$). The term neonates had substantially greater gestational age (38.31±1.00 vs 34.85±0.77 weeks), birth weight (3.06±0.26 vs 2.41±0.21 kg), cord ferritin levels (170.14±29.18 vs 110.57±23.17 ng/mL) and Apgar scores ($P<0.001$). There was a strong positive connection between cord serum ferritin and gestational age ($r=0.629$, $P<0.001$).

CONCLUSION: Our observations show that iron stores are reduced after delivery, as seen by considerably lower cord serum ferritin concentrations in late preterm infants compared with term infants. Ferritin levels in cord associated favorably with gestational age indicating that it may be an early marker of newborn iron status. Early detection may allow the timely monitoring and interventions to prevent the iron deficiency later.

KEYWORDS: Cord blood; Infant Fe status; Ferritin; Late preterm.

INTRODUCTION

Iron is a vital micronutrient that is involved in many cellular functions including oxidative energy metabolism, erythropoiesis and delivery of oxygen to bodytissues. It is important for early brain growth and function since it plays a role in neurogenesis, brain development and myelination. Fetal and neonatal iron insufficiency may severely impair cognitive and motor development during early life with long-lasting repercussions that are difficult to repair persisting into adulthood.[1,2] The high incidence of maternal anaemia, coupled with the fact that fetal iron supply relies only on maternal reserves and breast milk contains merely 0.03mg/dl of iron, underscores the significant challenge of iron shortage in babies.[3] It is crucial to preserve sufficient iron reserves during the perinatal and early childhood phases. On the other hand, an overabundance of iron poses a risk of producing harmful free radicals in premature infants who have diminished iron-binding proteins and underdeveloped antioxidant systems.[4–6] Fetal iron accretion occurs mostly during the third trimester of pregnancy; therefore, late preterm infants (34 to 36 weeks) are at greater risk than term infants of being born with depleted iron reserves. These newborns may appear clinically well at birth, but decreased iron stores may predispose them to iron insufficiency during infancy with deleterious effects on cognitive, motor, and neurodevelopmental outcomes.[7,8] Serum ferritin concentration in umbilical cord blood is a valid, non-invasive marker of neonatal iron reserves and correlates with fetal iron status at birth. The early diagnosis of infants with low cord ferritin concentrations facilitates nutritional management and adequate follow-up before the development of iron deficiency anaemia.[9,10]

The purpose of the study was to examine role of cord blood ferritin in predicting iron stores at term vs late preterm neonates between 34weeks – 36weeks

OBJECTIVES:
- To evaluate the role of role of cord blood ferritin in predicting iron stores at term vs late preterm neonates (34weeks-36weeks)
- To correlate the Iron stores in term and Late preterm neonates (34weeks to 36weeks).

METHODOLOGY:
The current hospital-based anlytical cross-sectional study was carried out in the Department of Paediatrics, SRM Medical College Hospital and Research Centre, Kattankulathur, Chengalpattu, Tamil Nadu, India over a duration of nine months from May 2025 to January 2026. All live-born neonates born in the hospital throughout the study period who were eligible were screened for recruitment. The enrolled neonates were divided into two groups based on gestational age:
Group I (Term neonates): 37 to 41 weeks gestation.
Group II (Late preterm neonates): Gestational age 34-36 weeks.
Sample size was calculated for comparison of two independent means using the following formula: n = (Z(1-a/2) + Z(1-b))2 (S.D2 + S.D2/r)/ (u1-u2)2 Where: Z(1-α/2)=1.96; Z(1-β)=0.84 corresponding to 80% study power; S1and S2 are standard deviations of cord ferritin in both groups; r=n2/n1(allocation ratio); (μ1-μ2)is expected mean difference in cord ferritin levels. The minimal sample size necessary was 96 newborns (48 term and 48 late preterm neonates) based on estimations from previous published studies.

INCLUSION CRITERIA:
- Neonates born between 34+0 and 41+6 weeks gestation.

EXCLUSION CRITERIA:
- Neonates had sepsis or shock at birth
- Neonates diagnosed with cyanotic heart disease, setting for Rh isoimmunization and major congenital malformation.
- Neonates born to mother had antepartum hemorrhage, acute bacterial or viral illness, chorioamnionitis, hemolytic disorder, received blood transfusion during antenatal period

ETHICAL CONSIDERATION: The ethical committee of the Institute approved the study (ID: EC/NEW/INST/2022/2933). The investigation was performed in conformity with "the Declaration of Helsinki".

DATA COLLECTION:
Subjects were recruited according to the inclusion criteria. The written consent was obtained from the mother of the study subjects. Demographic and clinical details of mother and neonate were recorded in a structured case record proforma. Maternal variables included age, parity, socioeconomic level, antenatal iron supplementationation, haemoglobin concentration at delivery, pregnancy associated problems, and mode of delivery. Neonatal variables included gestational age, sex, birth weight, Apgar scores, and NICU admission. Immediately after birth and before the separation of the placenta, approximately 3–5 mL of umbilical cord venous blood was aseptically collected. Immediately the samples were sent to the central laboratory for analysis. The haemoglobin concentration in cord blood was assessed using an automated hematology analyzer and the serum ferritin concentration was calculated by standardized chemiluminescent immunoassay (CLIA) accessible in the institutional central laboratory. Internal and external quality control measures were performed during the study.

STATISTICAL ANALYSIS:
Data were entered in Microsoft Excel 2021 and analyzed using IBM SPSS version 29.0. The continuous variables were checked for normality using the Shapiro-Wilk test and presented as mean ± standard deviation or median (interquartile range), as applicable. Categorical variables are reported as frequencies and percentages. Continuous factors were compared between term and late preterm neonates using independent samples t-test or Mann-Whitney U test, whereas categorical variables were compared using Chi-square test or Fisher's exact test. Two–tailed P value <0.05 was considered statistically significant.

RESULTS:

Table 1: MATERNAL CHARACTERISTICS

VARIABLES	CATEGORY	TERM	PRE-TERM	TOTAL	χ^2- value (p-value)
AGE (YEARS)	≤20	0	1	1	
	21-25	19	16	35	
	26-30	21	22	43	-

	30-35	8	9	17	
PARITY	PRIMI	23	21	44	0.240 (0.887)
	G2	17	18	35	
	G3 OR ABOVE	8	9	17	
IRON SUPPLEMENTATIONATION	TAKEN	43	42	85	0.105 (0.746)
	NOT TAKEN	5	6	11	
MATERNAL HB	<10.0	5	7	12	-
	10.0–10.9	12	15	27	
	11.0–11.9	19	17	36	
	≥12.0	12	9	21	
MODE OF DELIVERY	VD	29	21	50	-2.669 (0.102)
	LSCS	19	27	46	
MATERNAL COMPLICATIONS	None	28	27	55	0.174 (0.996)
	Pregnancy-induced hypertension	8	9	17	
	Gestational diabetes mellitus	6	6	12	
	Hypothyroidism	4	4	8	
	PROM	2	2	4	

Baseline maternal characteristics were similar between term and late preterm groups. Most mothers were in the age group of 26-30 years (44.8%) followed by 21-25 years (36.5%). 45.8% of the study population were primigravidae. 88.5% of women received antenatal iron supplementation. Most had a maternal haemoglobin level of 11.0–11.9 g/dL (37.5%). Slightly more were vaginal deliveries (52.1%) and 57.3% of women had no obstetric problems. None of the above maternal characteristics differed significantly between the two groups (P >0.05).

Table 2: NEW BORN CHARACTERISTICS

VARIABLES	CATEGORY	TERM	PRE-TERM	TOTAL	χ^2- value (p-value)
GENDER	Male	24	25	49	0.042 (0.838)
	Female	24	23	47	
BIRTH WEIGHT (KG)	<2.0	0	5	5	-
	2.0–2.49	5	31	36	
	2.5–3.5	42	12	54	
	>3.5	1	0	1	
CORD FERRITIN (ng/mL)	<75	1	6	7	-
	75 - 150	14	29	43	
	>150	33	13	46	
NICU ADMISSION	YES	2	11	13	7.194 (0.007*)
	NO	46	37	83	

Out of the 96 neonates, 51.0% (n=49) were males and 49.0% (n=47) were girls. Birth weight was considerably different between groups, with most late preterm neonates having 2.0–2.49 kg weight and most term neonates having 2.5–3.5 kg weight. Cord ferritin concentrations were substantially greater in term infants with 68.8% above 150 ng/mL as opposed to 27.1% of late preterm neonates. The rate of NICU admission was higher among late preterm newborns as compared to term neonates (22.9% vs. 4.2%). The difference shows the statistical significance (P- 0.007).

Table 3: DISTRIBUTION OF CONTINUOUS VARIABLES AMONG THE STUDY POPULATION

Variable	Term		Preterm		P-VALUE
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
Maternal age (years)	26.94±3.08	27 (23–31)	27.13±3.62	27.5 (21.0–32.0)	t= −0.277 (0.782)
Gestational age (weeks)	38.31±1.00	38.0 (37.0–39.0)	34.85±0.77	35.0 (34.0–36.0)	t=18.993 (<0.001*)
Birth weight (kg)	3.06±0.26	3.03 (2.86–3.2)	2.41±0.21	2.39 (2.26–2.57)	t=13.474 (<0.001*)

Maternal haemoglobin (g/dL)	11.91±1.05	11.65 (11.10–12.90)	11.89±1.01	11.80 (11.10–12.70)	t=0.095 (0.924)
Cord ferritin (ng/L)	170.14±29.18	178.05 (143.45–188.78)	110.57±23.17	110.35 (93.35–127.38)	<0.001*
1-minute Apgar score	8.04±0.76	8 (8–9)	6.83±0.83	7 (6–8)	<0.001*
5-minute Apgar score	9.56±0.49	9 (9–10)	9.19±0.76	9 (9–10)	<0.001*

Data are expressed as mean ± standard deviation (SD) and median (interquartile range, IQR). Independent-samples t-test was used for the comparisons of regularly distributed variables while Mann–Whitney U test was used for the comparisons of non-normally distributed variables (cord ferritin, Apgar score). There was no significant difference in maternal age and maternal haemoglobin levels between the two groups (26.94 ± 3.08 vs. 27.13 ± 3.62 years, P = 0.782 and 11.91 ± 1.05 vs. 11.89± 1.01 g/dL, P = 0.924 respectively). The mean GA (38.31 ± 1.00 vs. 34.85 ± 0.77 weeks; P < 0.001) and birth weight (3.06 ± 0.26 vs. 2.41 ± 0.21 kg; P < 0.001) of term neonates were substantially more than late preterm neonates. Cord ferritin concentrations were considerably greater in term infants (mean: 170.14 ± 29.18 µg/L; median (IQR): 178.05 (143.45–188.78) µg/L) than in late preterm neonates (mean: 110.57 ± 23.17 µg/L; median (IQR): 110.35 (93.35–127.38) µg/L) (P < 0.001). The 1-minute and 5-minute Apgar scores were also considerably higher in term infants compared with late preterm neonates.

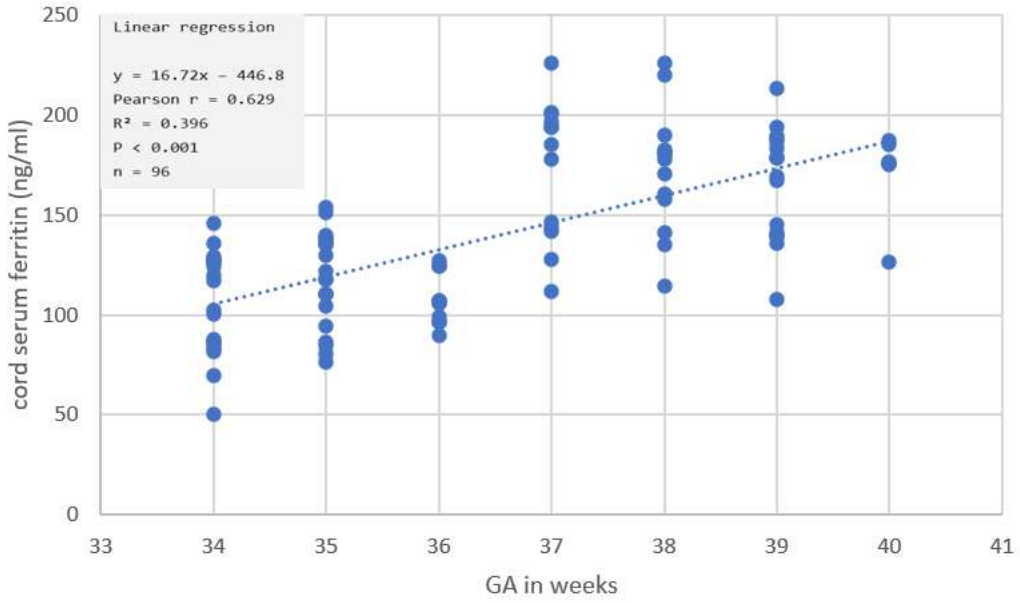

Figure 1: Correlation between gestational age and cord serum ferritin concentration among study neonates. There was a statistically significant positive association between the variables (r = 0.629, P < 0.001).

DISCUSSION

Iron metabolism experiences significant alterations in the final trimester and the early postnatal phase, a period when the infant is particularly vulnerable to both iron deficit and excess. Iron utilization throughout the neonatal phase is meticulously controlled, resulting in the majority of iron liberated from aging red blood cells being recycled, while the limited iron present in breast milk exhibits great bioavailability. Multiple maternal and neonatal factors can influence iron levels at delivery.[11,12] The aim of this study was to examine the cord ferritin concentrations in term and late preterm neonates to assess the neonatal iron reserves at birth.

MATERNAL FACTORS: The mean age of the term and preterm patients were 26.94±3.08 and 27.13±3.62 respectively. The most common age group of mothers was 26-30 years, 45.8% were primigravidae and 11.5% did not receive any iron supplementations. Vaginal deliveries were slightly more common in term neonates (29/48, 60.4%) whereas lower segment cesarean sections were more common in late preterm neonates (27/48, 56.3%). None of the above characters revealed

statistically significant differences between groups. There was no significant difference in maternal hemoglobin level between the groups with most women having hemoglobin levels between 11.0 and 11.9 g/dL. These results are consistent with the study by Celada et al. who found no significant correlation between maternal and cord blood ferritin levels suggesting that fetal iron transfer is a dynamic regulated mechanism not only dependent on maternal HB level.[13] Numerous prior investigations indicated that neonates exhibited markedly reduced haemoglobin and ferritin levels when the mother possessed critically diminished iron reserves.[14,15]

NEONATAL FACTORS: The gender distribution was similar between the term and late preterm groups in the current study with males comprising 50.0% of the term neonates and 52.1% of the late preterm neonates (P = 0.838). This suggests that the sex distribution was similar between the groups and unlikely to have contributed to the disparities in neonatal iron reserves reported. Similarly, Rao and Georgieff reported that the principal determinant of neonatal iron status is gestational maturity rather than sex.[8] The birth weight was significantly different between the two groups. Most of the late preterm neonates (64.6%) had a birth weight between 2.0 and 2.49 kg and most of the term neonates (87.5%) had a birth weight between 2.5 and 3.5 kg. This is consistent with previous observations that preterm newborns have lower birth weights because of shorter periods of intrauterine growth and represents the physiologic impact of shorter gestational age on fetal growth. Domellöf et al. have reported that birth weight and gestational age are major predictors of neonatal iron endowment and that newborns of lower birth weight had reduced total body iron reserves.[16] Late preterm neonates (22.9%) were considerably more likely to be admitted to NICU than term neonates (4.2%) (P = 0.007). Similar data have been reported by Engle et al, with much higher rates of NICU admission and newborn problems in late preterm infants than in term neonates.[17]
Although the increased NICU admission is a marker of increased clinical vulnerability of late preterm infants, the lower cord ferritin concentrations observed in this study are more likely due to incomplete fetal iron accretion due to shorter gestational age.

GESTATIONAL AGE: The main finding of this study was the significantly decreased ferritin concentration in the cord blood of late preterm neonates. 6 out of 7 subjects with ferritin level <75 ng/mL were from the late preterm cohort. The mean Ferritin concentration in the term group was noted to be 170.14±29.18 ng/mL, while in the preterm group it was 110.57±23.17 ng/mL. This is consistent with the assumption that most of the fetal iron accretion occurs in the third trimester; hence, infants born preterm are more sensitive to diminished iron stores. A statistically significant positive correlation was noted between gestational age and cord serum ferritin level ($r=0.629$, $P<0.001$) which shows that the longer the period of gestation, the higher the iron stores of the infant after birth. Our findings are in agreement with previous reports of increasing cord ferritin concentrations with gestational age, indicating that preterm infants have lower total cord ferritin than term infants.[9] Mean ferritin concentrations have also been demonstrated to rise with progressing gestational age across all groups, a finding corroborated by numerous other researchers.[18,19] Moreover, Pei et al. showed that gestational age is an independent predictor of cord ferritin, which increases with gestational age, especially in preterm newborns, confirming the importance of fetal maturity rather than maternal demographic characteristics as indicators of neonatal iron stores. Also, the study documented a non-linear correlation, suggesting a moment when placental iron transfer from mother to fetus diminishes, failing to keep pace with fetal iron absorption, ultimately leading to a net depletion of iron in the umbilical cord blood as gestational age advances.[1]

Neonates born late preterm had also a significantly higher rate of NICU admission and poorer Apgar scores at 1 and 5 min demonstrating their greater physiological vulnerability. Maternal haemoglobin levels were comparable across the two groups, indicating that in this cohort, newborn iron stores are mainly determined by gestational age and not by maternal iron status. Estimation of cord blood serum ferritin has significance that extends beyond only indicating fetal iron accumulation at delivery. Manifest anaemia in neonates is not anticipated nor detected at such an early stage of life, as some compensation arises from the physiological polycythemia characteristic of this period. Subsequently, as the polycythemia subsides, anaemia manifests due to their significant reliance on the maternal iron reserves obtained during gestation until the age of six months.[20] Previous studies have cited serum ferritin as the most reliable biochemical measure of body iron stores and it is extensively used to assess newborn iron status since it reflects total tissue iron reserves at delivery. Ferritin is able to detect iron reserves depletion before the onset of anaemia, therefore permitting an earlier identification of newborns at risk, unlike haemoglobin, which declines only in later stages of iron shortage. Cord serum ferritin is particularly useful as it is not altered by post-natal nutrition and gives a true measure of fetal iron endowment.[21,22] The present investigation showed that late preterm newborns had considerably lower cord serum ferritin concentrations than term neonates, indicating decreased iron reserves at delivery. Cord ferritin levels were significantly and positively correlated with gestational age, emphasizing the importance of third-trimester placental iron transport in fetal iron accretion. The groups were equal in terms of maternal age, parity, iron supplementationation, maternal haemoglobin, mode of delivery and maternal problems. However, late preterm neonates had a considerably lower birth weight, poorer Apgar score, and greater rates of NICU admissions.
Our findings, meanwhile, are constrained by a limited sample size. Also, no further follow up was done in our study. Another limitation is that it is a single-center investigation and may not accurately reflect the broader research population.

CONCLUSION

In conclusion, our data suggest that cord ferritin is a good marker of iron status in the neonate and emphasize the increased susceptibility of late preterm newborns to iron depletion. These results underline the need of early diagnosis of neonates with low iron stores, allowing adequate nutritional management and follow-up to avoid eventual iron deficiency and its deleterious consequences on growth and neurodevelopment. Further investigation is required with large sample size and follow up to explore the correlation and the underlying physiological mechanisms.

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