

Abstract

- Iron deficiency (ID) is common in very low birth weight (VLBW) neonates, contributing to long-term neurodevelopmental impairments.
- Premature infants, particularly those born VLBW, are at high risk, with up to 17% showing ID at birth.
- Current diagnostic methods, including serum ferritin and transferrin saturation (TS), are unreliable due to factors like inflammation and diurnal variation.
- This retrospective study aimed to assess ID in VLBW infants using reticulocyte hemoglobin equivalent (Ret-He) as a screening tool.
- Of 103 eligible infants, 31% had low Ret-He, and 86.7% of those with low Ret-He met one or more ID criteria.
- Ret-He is a useful early indicator for diagnosing ID in VLBW neonates.

Introduction

- Iron plays a vital role in the development of the central nervous system.
- During ID, iron supply for blood cell production is prioritized over other organs such as the brain (1).
- Fetal and early postnatal iron deficiency (ID) is associated with acute and long-term neurodevelopmental and neurobehavioral abnormalities (2).
- VLBW infants are at high risk for ID. Hence, it is crucial to identify and treat ID in the immediate neonatal period.
- Currently, there are no standardized guidelines for diagnosing ID in the neonatal population (3).
- Ret-He is an early indicator of ID and is recommended by AAP as a screening tool for ID.
- We aim to determine the incidence of ID in VLBW infants at birth as evidenced by low Ret-He and abnormal iron studies.

Methods

- This is a retrospective chart review of all VLBW infants born between 10/2021 and 01/2024.
- The data on complete blood count (CBC) and reticulocyte studies performed during the first few days of life were collected from medical records.
- Low Ret-He is defined as ≤ 29 pg.
- All infants with Ret-He ≤ 29 had iron studies performed based on our unit protocol- serum iron, transferrin saturation (TS) and ferritin.
- Infants with low Ret-He were compared with those with normal Ret-HE.
- Iron deficiency was defined as serum iron < 100 mcg/dL, transferrin saturation $< 30\%$, or serum ferritin < 50 ng/ml.
- Infants with Hemoglobin Barts (Hb Barts) were excluded.

Results

- A total of 109 infants were born during the study period with a CBC with retic count performed after birth.
- 6 infants with Hb Barts positive newborn screen were excluded from the analysis
- The demographic characteristics are depicted in Table 1.
- 32 infants had Ret-He ≤ 29 (31%) at birth.
- In the low Ret-He group, median hemoglobin was 14.4 g/dL, median Ret-He was 26 pg, median serum iron was 69 mcg/dL, median ferritin was 236 ng/ml, and median transferrin saturation was 25%.
- Iron studies were performed in 30 infants. 26 infants (86.7%) with low Ret-He had at least one of the criteria for ID.
- Interestingly, 28 out of 29 infants had normal or elevated serum ferritin levels.

Table 1: Demographics and risk factors

Demographics and Risk factors	Normal Ret-He group (n=71)	Low Ret-He group (n=32)	p-value
Male infants (%)	28 (39.4)	15 (46.9)	0.48
Delayed cord clamping (%)	32 (45.1)	12 (37.5)	0.03
Cesarean delivery (%)	52 (73.2)	23 (71.9)	0.77
Small for gestational age (%)	18 (25.3)	7 (21.9)	0.57
Maternal Hypertension (%)	27 (38)	11 (34.4)	0.87
Maternal Diabetes (%)	6 (8.5)	8 (25)	0.07
Maternal Antepartum hemorrhage (%)	4 (5.6)	0 (0)	0.25
Maternal Obesity (%)	25 (35.2)	16 (50)	0.37
Maternal Smoking (%)	10 (14.1)	5 (15.6)	0.62
Maternal Alcohol (%)	4 (5.6)	0 (0)	0.24
Maternal anemia (%)	36 (50.7)	18 (56.3)	0.61

Table 2: Comparison between two groups (median, IQR)

Characteristics	Normal Ret-He group (n=71)	Low Ret-He group (n=32)	p-value
Gestational Age	29.1 (26.5- 31.1)	28.8 (25.7-31.0)	0.63
Birth Weight (g)	980 (785-1318)	940(786-1231)	0.64
Hemoglobin(g/dL)	15.8(13.0-18.5)	14.5(11.8-16.5)	0.034
Hemoglobin < 13.5 g/dl (%)	18 (25.4)	12 (37.5)	0.21
Hematocrit (%)	45.1 (38.5-52.2)	43.0(35.9-49.3)	0.11
Retic Percentage (%)	7.7 (5.5-10.3)	6.5(4.2-8.5)	0.021
Immature Retic Fraction	44.4(39.4-50.0)	41.8(32.53-47.33)	0.09
Retic Hgb Equivalent (pg)	32.9 (31.2-34.6)	26.0(25.2-27.9)	<0.001

Discussion

- Low Ret-He was present in 31% of the VLBW infants at birth. 86.7% infants had evidence of low iron.
- Ret-He can be used to screen for ID in VLBW infants.
- Identifying ID at birth and providing appropriate treatment may prevent long term neurocognitive impairment in VLBW infants.
- Further studies are needed to assess if Ret-He can be utilized to guide iron therapy to improve iron status in VLBW infants.

References

1. Zamora TG, Guiang SF, Widness JA, Georgieff MK. Iron is prioritized to red blood cells over the brain in phlebotomized anemic newborn lambs. *Pediatric Research*. 2016;79(6):922-8.
2. Georgieff MK. Iron deficiency in pregnancy. *American Journal of Obstetrics and Gynecology*. 2020;223(4):516-24.
3. Christensen RD, Bahr TM, Ward DM. Iron Deficiency in Newborn Infants: Global Rewards for Recognizing and Treating This Silent Malady. *Newborn*. 2022;1(1):97-103.