Prevalence of Iron Deficiency in Infants of Diabetic Mothers Using Reticulocyte Hemoglobin Equivalent

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Abstract

- Fetal and early postnatal iron deficiency (ID) is linked to neurodevelopmental and neurobehavioral abnormalities.
- Low reticulocyte hemoglobin equivalent (Ret-He) serves as a screening tool for ID.
- This prospective study analyzed cord blood samples from infants of diabetic mothers (IDM) and no-risk infants, focusing on hematological indicators.
- Findings suggest a higher prevalence of low Ret-He and associated iron deficiency in IDM infants, underscoring the importance of identifying and managing ID at birth to help prevent potential long-term effects.

Introduction

- Iron plays a vital role in the development of the central nervous system including cell division, neuronal growth, dendrite branching, myelination, and neurotransmitter production.
- ID in the critical period of rapid brain growth can result in declines in cognitive functions and neurodevelopment.[1]
- Maternal diabetes is a major risk factor for ID.[2]
- Maternal diabetes can cause fetal hypoxia, increased erythropoiesis and increase iron demand, making it a risk factor for ID in the neonatal population.
- Serum ferritin is an acute phase reactant and can be affected by infection and inflammation. Transferrin saturation (TS) can have diurnal variation.
- Ret-He is an early marker of ID
- This study aims to determine the prevalence of ID in infants of diabetic mothers (IDM) by assessing Ret-He.

Methods

- Prospective Observational Cohort Study at Thomas Jefferson University Hospital (TJUH), Philadelphia. PA.
- Pregnant women admitted to the labor and delivery unit were screened and informed consent was obtained.
- Cord blood samples were collected at the time of delivery and sent to the lab for analysis .
- Complete blood count, reticulocyte count, and serum iron studies were performed.
- Maternal and infant characteristics were collected from the medical records.
- The clinical and hematological characteristics of IDM neonates were compared with no risk factors for ID (no-risk group).
- Low Ret-He was defined as <31 pg.

Results

- A total of 399 samples were collected from May 2021 till September 2024.
- There were 52 IDM infants and 81 infants in the no-risk group.
- The clinical characteristics are displayed in Table 1 and the hematologic characteristics are depicted in Table 2.
- Among the IDM group, 6 infants (11.5%) had Ret-He <31 pg with a range from 18.5 pg - 29.7 pg.
- Among no-risk group, 4 infants (4.9%) had Ret-He <31 pg with a range from 28.7 pg - 29.5 pg.
- The IDM group had significantly lower Ret-He and lower serum ferritin
- Red cell distribution width was higher in IDM compared to the no-risk group.

Table 1: Clinical Characteristics

Characteristics	IDM (n=52)	No risk group (n=81)
Birth weight in grams (med, IQR)	3260 (3020-3555)	3310 (3035,3540)
Gestational age in weeks (med, IQR)	38 (37.1-39.1)	39.4 (38.5-40.1)
Preterm <37 weeks (n, %)	8 (15%)	5 (6%)
Small for gestational age (n, %)	6 (11%)	6 (7%)
Large for gestational age (n, %)	7 (13.4%)	7 (8.6%)
Race, Black (n, %)	24 (46%)	9 (11%)
Sex, Male (n, %)	33 (65%)	44 (54%)
Vaginal delivery (n, %)	21 (40%)	58, (72%)
Delayed cord clamping	39 (73.5%)	58 (71.6%)

Table 2: Hematological parameters

Hematological parameters	IDM (n=52)	No risk group (n=81)	P Value
Hemoglobin g/dL (med, IQR)	15.5 (14.3-16.4)	15.3 (14-16.3)	0.29
Hematocrit % (med, IQR)	46.5 (43.6-58.7)	45.3 (42.6-48.4)	0.27
Mean corpuscular volume (med, IQR)	106.5 (102.8-110.3)	107 (104-111)	0.32
RDW, % (med, IQR)	**17.2 (16.2-17.8)**	**16.5 (15.9-17.3)**	**0.003**
Reticulocyte count (med, IQR)	4.2 (3.78-4.7)	4.4 (3.8-4.8)	0.9
Ret-He in pg (mean, IQR)	**32.9 (31.7-34.6)**	**33.9 (32.7-35.2)**	**0.027**
Serum Iron mcg/dL (med, IQR)	142 (118-177)	135 (112-163)	0.16
TS % (med, IQR)	55.5 (39.5-74.8)	60 (48-73)	0.95
Ferritin ng/ml (med, IQR)	**143.5 (89.8-226.8)**	**222 (152-301)**	**0.003**
Infants with Ret-He <31 pg, n (%)	6 (11.5%)	4 (4.9%)	0.41

Discussion

- Low Ret-He was present in 11.5% of IDM neonates suggesting they were iron deficient. This finding aligns with previous research demonstrating that IDM are at risk for ID.
- The significant difference in mean Ret-He between the IDM group compared to the no-risk group highlights the need for early iron deficiency screening in IDM.
- Identifying and addressing ID at birth may help prevent the long-term negative cognitive effects associated with neonatal iron deficiency, particularly in vulnerable populations.

References

1. Collard KJ. Iron homeostasis in the neonate. *Pediatrics*. 2009;123(4):1208–1216.
2. McLimore HM, Phillips AK, Blohowiak SE, Pham DQ, Coe CL, Fischer BA, Kling PJ. Impact of multiple prenatal risk factors on newborn iron status at delivery. J Pediatr Hematol Oncol. 2013 Aug;35(6):473-7.
3. Riggins T, Miller NC, Bauer PJ, Georgieff MK, Nelson CA. Consequences of low neonatal iron status due to maternal diabetes mellitus on explicit memory performance in childhood. Dev Neuropsychol (2009) 34(6):762–79.