To Study the Iron Status at Birth in Neonates with Risk Factors to Develop Iron Deficiency Anemia

[1]Dr.K Sandeep Kumar, [2]Dr. R P S Tomar, [3]Dr.Gururaja R

[1]Pediatrican, Base Hospital Delhi Cantt, New Delhi
[2]Professor of Paediatrics, Base Hospital, Delhi Cantt, New Delhi
[3]Assistant Professor, Department of Paediatrics, Command Hospital, Lucknow, Uttar Pradesh

CorrespondingAuthor : Dr.Gururaja. R,

ABSTRACT

Background: The newborn stage is very demanding and stressful. With the transition of the baby baby from the intra uterine to the extra uterine environment, numerous physiological adaptations take place. While in-utero, the baby received nutrients and metabolic substrates through the umbilical cord, extra-uterine survival requires an interaction between substrates stored in-utero and substrates acquired post-natally.

Methods

This was an observational cross-sectional study was during the period of 12 months (January 2021 till December 2021) in Newborn intensive Care Unit (NICU) and Post natal ward which is attached to NICU at Department of Paediatrics at Base hospital, Delhi Cantt. The study protocol conforms to the Declaration of Helsinki and was approved by the Institutional Ethics Committee before commencement.

Results

We observed that among IDM, mean cord hemoglobin was 16.17 ± 1.63 gm/dl, mean cord iron level was 156.9 ± 30.74 mcg/dl, mean cord ferritin was 71.8 ± 21.37 ng/ml and mean TIBC was 311.6 ± 63.16 mcg/dl. We observed that among IDM, 6.3% had low cord blood hemoglobin, 6.3% had low cord blood iron, 3.1% had low cord blood ferritin and 6.3% had high TIBC. Among VLBW neonates, mean cord hemoglobin was 15.41 ± 2.5 gm/dl, mean cord iron level was 141.7 ± 35.47 mcg/dl, mean cord ferritin was 65.95 ± 27.7 ng/ml and mean TIBC was 340.7 ± 71.6 mcg/dl. We observed that 9.1% had low cord blood hemoglobin, 18.2% had low cord blood iron, 13.6% had low cord blood ferritin and 18.2% had high TIBC.

Conclusion

Our current data indicate that some newborns are definitely iron deficient. Our findings support a more individualized approach to iron supplementation in infants. The measurement of cord blood iron parameters in neonates at risk at the moment of birth is necessary to detect any iron deficiency. In addition, newborns with low serum ferritin should have their iron status closely monitored.

Keywords: Newborn, Hemoglobin,Anemia.

DOI Number: 10.48047/nq.2023.21.6.NQ23151 **NeuroQuantology2023;21(6): 1490-1501**

INTRODUCTION

The newborn stage is very demanding and stressful. With the transition of the baby from the intra uterine to the extra uterine environment, numerous physiological adaptations take place. While in-utero, the baby received nutrients and metabolic substrates through the umbilical cord, extra-uterine survival requires an interaction between substrates stored in-utero and substrates acquired post-natally. These are essential to satisfy the metabolic demands of development and growth. Iron is one such substrate.[1] Iron is an important micronutrient that plays a crucial role in cellular organ system functioning, especially in the early growth and

development of the brain. To achieve their daily iron needs and maintain a neutral iron balance, neonates rely on in-utero iron accumulation and post-natal external consumption. As both negative and positive iron balances are detrimental to biological processes, it is essential to maintain a neutral iron balance.[2]

Transplacental iron accumulation begins at the earliest at 24 weeks gestation and continues throughout pregnancy. The majority of iron accumulation however, occurs during the third trimester, being directly proportionate to gestational age.[3] Thus, since preterm infants are delivered before the majority of placental iron accumulation, they are at risk for iron deficiency. In the absence of iron supplementation, the increased growth rate and subsequent increase in cell mass that happens as part of catch-up development in preterm infants exacerbate these already depleted iron reserves.

Starting in the second week of life, iron supplementation at a rate of 2-4 mg/kg/day may prevent iron deficiency in preterm infants without the danger of iron overload. Iron accumulation is also impacted by a number of other variables.

Intrauterine variables like maternal iron supplementation, female gender, and fetofetal transfusion (receiver twin) provide a positive iron balance. In contrast, intrauterine variables such as severe maternal iron shortage, maternal diabetes, maternal smoking, intra-uterine growth restriction (IUGR), preterm delivery, and low birth weight result in a negative iron balance.[4]In the absence of additional intrauterine variables, however, preterm delivery and low birth weight are the most major causes of diminished iron reserves. In contrast, milk (breast/formula), early iron supplementation, and recurrent blood transfusion are postnatal variables that contribute to a positive iron balance. These may result in iron overload, which, particularly in preterm infants, increases bacterial colonization and generates Reactive Oxygen Species (ROS), leading to problems such bronchopulmonary dysplasia and retinopathy of prematurity.[5] A negative iron balance postnatally is caused by phlebotomy, persistent gastrointestinal hemorrhage, increased intravascular hemolysis from sepsis, a shorter fetal red blood cell lifetime, low circulating erythropoietin levels, and restricted transfusion protocols.

Ferritin is the primary iron storage protein, and its blood levels are the benchmark for assessing iron reserves in preterm infants. These levels are exclusively lowered in iron shortage, with a serum ferritin level of less than 35 g/l serving as the cutoff for premature infants. In contrast, serum ferritin levels are raised after infection, inflammation, and malignant transformation. Iron insufficiency might be obscured by its increased levels under certain settings.[6]

The assessment of newborn iron reserves using ferritin is justified by the hierarchical nature of tissue iron loss. In the context of iron shortage, red blood cell (RBC) iron for hemoglobin production takes precedence over iron reserves in the brain, heart, and skeletal muscle. Therefore, by the time serum iron deficiency is determined, iron reserves are already exhausted.

Several risk factors for iron insufficiency in early childhood have been identified. These include small for gestational age neonates (SGA, birth weight 10th percentile), newborns of diabetes mothers (IDM), and very low birth weight preterm neonates (VLBW, birth weight 1500 grammes).[7]Chronicfetal hypoxia and decreased iron transfer from the mother to the fetus may lead to iron deficit in SGA or IDM newborns. Preterm infants do not get the benefit of the massive iron accumulation that typically happens during the third trimester of pregnancy, resulting in an elevated risk of iron shortage at delivery.

In light of this, we examined the iron status at delivery in high-risk neonates with risk factors for iron deficiency anemia in the current research.

MATERIAL AND METHODS

AIM AND OBJECTIVES

Aim

The aim of the study was to examine the iron status at birth in high risk neonates who have risk factors to develop iron deficiency anemia.

Objectives

- To assess cord blood iron status in small-for-gestational age neonates.
- To assess cord blood iron status in very low birth weight neonates.
- To assess cord blood iron status in infants of diabetic mothers.
- To identify various maternal and neonatal factors associated with iron deficiency in these neonates.

The was an observational cross-sectional study was during the period of 12 months (January 2021 till December 2021) in Newborn intensive Care Unit (NICU) and Post natal ward which is attached to NICU at Department of Paediatrics at Base hospital, Delhi Cantt. The study protocol conforms to the Declaration of Helsinki and was approved by the Institutional Ethics Committee before commencement. Written informed consent was taken from all parents. No harm is intended for the subjects. A prick pain was experienced during the withdrawal of the blood sample. The same was explained to the parents before consenting. The study participants were not subjected to any extra cost because of the study.

INCLUSION CRITERIA

We included healthy as well as hospitalized neonates who are at high risk of developing iron deficiency anemia. High-risk group was defined as:
Very low birth weight (VLBW) infants (1000 to 1500 gm)
Asymmetric term Small for Gestational Age (SGA) (birth weight <10th
percentile for gestational age)
Infants of diabetic mother (IDM)
The weight of infant was classified into percentiles based on the Indian standards for birth weights of newborns based on the sex and order of the baby.[8]

EXCLUSION CRITERIA
Extreme low birth weight (< 1000 gm).
Extreme premature neonates (<28 weeks)
Neonates having major congenital malformations.
Twin pregnancy neonates
Neonates of mothers with history of abruption placenta.

SAMPLING
MacQueen et al (2019)found biochemical iron deficiency at birth in 13% of the screened neonates (SGA, IDM and VLBW neonates).[9] Sample size was calculated using the following formula:

$N = (Z_{\alpha/2})^2 * (PQ) / E^2$
N = Sample size
$Z_{\alpha/2}$ = Z value at confidence level of 99% (2.58)
= Taken as 13%
= 1-P
E = Allowable error taken as 10%
$N = \underline{(2.58)^2 * (0.13*0.87)}$
$(0.1)^2$
N = 75.3
So a minimum of 75 consecutive neonates were included in the study.

STATISTICAL ANALYSIS
The analysis included profiling of patients on different demographic, laboratory and clinical parameters. Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Ordinal data were expressed as absolute number and percentage. Iron deficiency anemia was diagnosed in neonates who had low hemoglobin, low ferritin and high TIBC. Various parameters were compared between neonates with iron deficiency anemia and those without iron deficiency anemia. Cross tables were generated and chi square test was used for testing of associations Student t test was used for comparison of quantitative parameters. P-value < 0.05 is considered statistically significant. All analysis were done using SPSS software, version 24.0.

RESULTS

Risk factor category	Frequency	Percent
Infant of diabetic mother	32	42.7
Very low birth weight	22	29.3
Small for gestational age	21	28
Total	75	100

Table 1. Distribution of neonates according to their risk factor category

In the present study, 75 neonates fulfilling the study criteria were included. Of these, 42.7% were Infant of diabetic mother, 29.3% were very low birth weight and 28% were small for gestational age.

Description of cord blood iron indices in infants of diabetic mother (n=32)				
Cord blood iron indices in IDM Cord hemoglobin	Minimum	Maximum	Mean	Std. Deviation
(gm/dl)	9.80	17.10	16.17	1.63
Cord Iron (mcg/dl)	78.00	202.00	156.91	30.74
Cord ferritin (ng/ml)	19.00	99.00	71.88	21.37
TIBC (mcg/dl)	188.00	500.00	311.69	63.16
Description of cord blood iron indices in very low birth weight baby (n=22)				
Cord blood iron indices in VLBW Cord hemoglobin	Minimum	Maximum	Mean	Std. Deviation
(gm/dl)	8.90	17.00	15.41	2.50
Cord Iron (mcg/dl)	81.00	197.00	141.77	35.47
Cord ferritin (ng/ml)	21.00	112.00	65.95	27.70
TIBC (mcg/dl)	250.00	490.00	340.73	71.68

We observed that among IDM, mean cord hemoglobin was 16.17 ± 1.63 gm/dl, mean cord iron level was 156.9 ± 30.74 mcg/dl, mean cord ferritin was 71.8 ± 21.37 ng/ml and mean TIBC was 311.6 ± 63.16 mcg/dl. Among VLBW neonates, mean cord hemoglobin was 15.41 ± 2.5 gm/dl, mean cord iron level was 141.7 ± 35.47 mcg/dl, mean cord ferritin was 65.95 ± 27.7 ng/ml and mean TIBC was 340.7 ± 71.6 mcg/dl.

Cord blood iron indices in SGA Cord hemoglobin	Minimum	Maximum	Mean	Std. Deviation
(gm/dl)	10.00	17.10	15.89	1.85
Cord Iron (mcg/dl)	92.00	201.00	149.19	36.68
Cord ferritin (ng/ml)	18.00	109.00	68.90	23.15
TIBC (mcg/dl)	232.00	495.00	318.48	63.71

Table 4. Description of cord blood iron indices in small for gestational age neonate (n=21)

Among SGA neonates, mean cord hemoglobin was 15.89 ± 1.85 gm/dl, mean cord iron level was 149.19 ± 36.68 mcg/dl, mean cord ferritin was 68.9 ± 23.15 ng/ml and mean TIBC was 318.48 ± 63.71 mcg/dl.

Cord Iron profile parameters Cord blood hemoglobin	IDM (n=32)	VLBW (n=22)	SGA (n=21)	Total (n=75)
Low	2 (6.3%)	2 (9.1%)	1 (4.8%)	5 (6.7%)
Normal Cord blood iron	30(93.8%)	20 (90.9%)	20 (95.2%)	70 (93.3%)
Low	2 (6.3%)	4 (18.2%)	1 (4.8%)	7 (9.3%)
Normal Cord blood ferritin	30(93.8%)	18 (81.8%)	20 (95.2%)	68 (90.7%)
Low	1 (3.1%)	3 (13.6%)	1 (4.8%)	5 (6.7%)
Normal Cord blood TIBC	31(96.9%)	19 (86.4%)	20 (95.2%)	93.3%)
High	2 (6.3%)	4 (18.2%)	2 (9.5%)	8 (10.7%)
Normal	30(93.8%)	18 (81.8%)	19 (90.5%)	67 (89.3%)

Table 5. Distribution of neonates according to their risk factor category and cord blood indices

When we distributed neonates according to their risk factor category, we observed that among IDM, 6.3% had low cord blood hemoglobin, 6.3% had low cord blood iron, 3.1% had low cord blood ferritin and 6.3% had high TIBC. Among VLBW neonates, we observed that 9.1% had low cord blood hemoglobin, 18.2% had low cord blood iron, 13.6% had low cord blood ferritin and 18.2% had high TIBC. Among SGA neonates, we observed that 4.8% had low cord blood hemoglobin, 4.8% had low cord blood iron, 4.8% had low cord blood ferritin and 9.5% had high TIBC.

Iron deficiency anemia in neonate	Frequency	Percent
Yes	5	6.7
No	70	93.3
Total	75	100

Table 6. Distribution of neonates according to iron deficiency anemia

Based on the hematological criteria of diagnosing iron deficiency anemia (low hemoglobin, low ferritin and high TIBC), 5 neonates in our sample (6.7%) had iron deficiency anemia.

		Iron deficiency anemia in neonate		Total
Maternal age (years)		No	Yes	
18 to 20	N	2	1	3
	%	2.90%	20.00%	4.00%
21 to 30	N	53	3	56
	%	75.70%	60.00%	74.70%
31 to 40	N	15	1	16

	%	21.40%	20.00%	21.30%
Total	N	70	5	75
	%	100.00% 100.00% p value* = 0.16		100.00%
Mean maternal age (years)		26.8 ± 4.03 26.2 ± 7.5 p value** = 0.76		

Table 7. Association of iron deficiency anemia in neonate and maternal age

*analyzed using chi-square test; **analyzed using independent t test

We observed that 74.7% of the mothers were aged 21 to 30 years. Mean age of the mothers with iron deficiency anemia neonate was 26.2 years, while that of neonates without no iron deficiency anemia was 26.8 years. We observed that iron deficiency anemia in neonate was not significantly associated with maternal age (p value = 0.16).

			Iron deficiency anemia in neonate		Total
Gravid			No	Yes	
Multigravida		N	44	2	46
		%	62.90%	40.00%	61.30%
Primigravida		N	26	3	29
		%	37.10%	60.00%	38.70%
Total		N	70	5	75
		%	100.00% 100.00% p value* = 0.31		100.00%

Table 8. Association of iron deficiency anemia in neonate and gravidity

analyzed using chi-square test

Among the 5 neonates with iron deficiency anemia, two were born to multigravida mothers and three to primigravida mothers. Gavida status of the mother was not significantly associated the iron deficiency anemia (p value = 0.31).

		Iron deficiency anemia in neonate		Total
Gestational period		No	Yes	
Very preterm	N	14	1	15
	%	20.00%	20.00%	20.00%
Early preterm	N	5	2	7
	%	7.10%	40.00%	9.30%
Late preterm	N	22	1	23
	%	31.40%	20.00%	30.70%
Early term	N	27	1	28
	%	38.60%	20.00%	37.30%
Full term	N	2	0	2
	%	2.90%	0.00%	2.70%
Total	N	70	5	75
	%	100.00% 100.00% p value* = 0.18		100.00%

Table 9. Association of iron deficiency anemia in neonate and gestational period

*analyzed using chi-square test

Among the 5 neonates with iron deficiency anemia, one was very preterm, two were early preterm, one was later pretem and one was early term. Gestational period was not significantly associated with iron deficiency anemia (p value = 0.18).

Table 10. Association of iron deficiency anemia in neonate and maternal anemia

Iron deficiency anemia in
Total
neonate

Maternal anemia		No	Yes
Yes	N	8	1	9
	%	11.40%	20.00%	12.00%
No	N	62	4	66
	%	88.60%	80.00%	88.00%
Total	N	70	5	75
	%	100.00%	100.00%	100.00%
p value = 0.56				
Mean maternal hemoglobin (gm%)		11.9 ± 1.02	11.98 ± 0.85	
p value = 0.98				

*analyzed using chi-square test; **analyzed using independent t test

Among the 5 neonates with iron deficiency anemia, mother of only one had anemia. Maternal anemia was not found to be significantly associated with iron deficiency anemia (p value = 0.56).

		Iron deficiency anemia		
Obstetric history of iron		in neonate		Total
supplementation		No	Yes	
Yes	N	66	5	71
	%	94.30%	100.00%	94.70%
No	N	4	0	4
	%	5.70%	0.00%	5.30%
Total	N	70	5	75
	%	100.00%	100.00%	100.00%
		p value = 0.58		

Table 11. Association of iron deficiency anemia in neonate and obstetric history of iron supplementation

*analyzed using chi-square test

Among the 5 neonates with iron deficiency anemia, all five have maternal history of iron supplementation during the antenatal period (p value = 0.58).

		Iron deficiency anemia in neonate		Total
Risk factor category		No	Yes	
Infant of diabetic mother	N	31	1	32
	%	44.30%	20.00%	42.70%
Small for gestational age	N	20	1	21
	%	28.60%	20.00%	28.00%
Very low birth weight	N	19	3	22
	%	27.10%	60.00%	29.30%
Total	N	70	5	75
	%	100.00%	100.00% p value* = 0.28	100.00%

Table 12. Association of iron deficiency anemia in neonate and risk factor category

*analyzed using chi-square test

We observed that among the 5 neonates with iron deficiency anemia, one was IDM, one was SGA and three were VLBW. We observed that risk factor category was not significantly associated with iron deficiency anemia (p value = 0.28).

		Iron deficiency anemia in neonate		Total
Sex of new born		No	Yes	
Female	N	36	2	38
	%	51.40%	40.00%	50.70%
Male	N	34	3	37
	%	48.60%	60.00%	49.30%
Total	N	70	5	75
	%	100.00%	100.00%	100.00%
		p value* = 0.62		

Table 13. Association of iron deficiency anemia in neonate and sex of the new born

*analyzed using chi-square test

Among the 5 neonates with iron deficiency anemia, three were males and rest two were females. Sex of the new born was not significantly associated with iron deficiency anemia (p value = 0.62).

		Iron deficiency anemia in neonate
		No Yes
Mean birth weight (kg)		2.31 ± 0.77 1.98 ± 0.99
		p value* = 0.36

Table 14. Association of iron deficiency anemia in neonate and mean birth weight

*analyzed using independent t test

Mean birth weight of neonates with iron deficiency anemia was 1.98 ± 0.99 kgs, which was not significantly different from that of those without iron deficiency anemia (2.31 ± 0.77 kg), p value = 0.36.

DISCUSSION

We included healthy as well as hospitalized neonates who are at high risk of developing iron deficiency anemia. High-risk group was defined as VLBW infants (1000 to 1500 gm), asymmetric term SGA and IDM. Of the sample of 75 neonates, 42.7% were Infant of diabetic mother, 29.3% were very low birth weight and 28% were small for gestational age. The aim of the study will be to examine the iron status at birth in high risk neonates who have risk factors to develop iron deficiency anemia. The results of our study are discussed as follows.

Cord blood indices in IDM

We observed that among IDM, mean cord hemoglobin was 16.17 ± 1.63 gm/dl, mean cord iron level was 156.9 ± 30.74 mcg/dl, mean cord ferritin was 71.8 ±

21.37 ng/ml and mean TIBC was 311.6 ± 63.16 mcg/dl. We observed that among IDM, 6.3% had low cord blood hemoglobin, 6.3% had low cord blood iron, 3.1% had low cord blood ferritin and 6.3% had high TIBC.

El-Raggal et al. performed a research to investigate the impact of maternal diabetes on fetal iron status measures, including STfR, ferritin levels, and their ratio (TfR-F index), in cord blood samples from newborns with and without maternal diabetes.[10] Their findings indicated that infants of diabetic mothers (IDM) had significantly lower iron stores, as indicated by lower s.ferritin (P=0.000) and significantly higher serum transferring receptors(STfR) levels than infants born to the control mothers (P=0.038). Additionally, the higher sTfR level in insulin-dependent diabetes mellitus (IDDM) mothers suggested an increased erythropoiesis state.

In a similar research, Verner et al. reported that maternal diabetes depleted fetal iron reserves and was linked with increased fetal iron needs, as demonstrated by a higher STfR (P < 0.01) level and TfR- F index (P< 0.01) in cord blood of IDM compared to cord blood of children born to non-diabetic mothers.[11]

Hashim et al. wanted to determine the influence of maternal diabetes on cord blood serum ferritin in a separate investigation.[12]There was a very significant difference in serum ferritin levels between newborns of diabetes and healthy mothers; the IDM and control groups had mean serum ferritin levels of 53.393 ng/ml and 105.522 ng/ml, respectively.

Maternal BMI, diabetes, and birth weight z score are three interdependent, interaction variables; hence, future research should investigate the relative significance of each in a biological etiology. Lesser et al. discovered that the aberrant iron status in neonates delivered to mothers with insulin-dependent diabetes was caused by a lack of supply owing to dysfunctional placental transport, which was aggravated by increased demand due to faster growth and bigger blood

volumes.[13] These results support the findings of Petry et al., who established that transferrin receptors on the placentae of diabetes women are defective and unable to compensate for the iron deficiency in the fetal compartment.[14]

The study by McLimore et al extends these findings from frank diabetes to noninsulin-dependent gestational diabetes, a concerning finding given the prevalence of obesity among women of childbearing age and the known association between maternal obesity at conception, gestational diabetes, and the likelihood of giving birth to LGA newborns.[15]

Cord blood indices in VLBW

Among VLBW neonates, mean cord hemoglobin was 15.41 ± 2.5 gm/dl, mean cord iron level was 141.7 ± 35.47 mcg/dl, mean cord ferritin was 65.95 ± 27.7 ng/ml and mean TIBC was 340.7 ± 71.6 mcg/dl. We observed that 9.1% had low cord blood hemoglobin, 18.2% had low cord blood iron, 13.6% had low cord blood ferritin and 18.2% had high TIBC. In addition, mean birth weight of neonates with iron deficiency anemia was 1.98 ± 0.99 kgs, which was not significantly different from that of those without iron deficiency anemia (2.31 ± 0.77 kg), p value = 0.36.

El-Raggal demonstrated a significantly significant birth weight difference between IDMs and the control group. The mean birth weight of IDMs was 3.87 ± 0.41g, while the mean birth weight of the control group was 3.34 ±0.30g ($p < 0.001$). This is consistent with the findings of Ceitin et al., who found that newborns in the healthy control group had a birth weight (g) of 3356 ±174 compared to 3936 ± 681 for IDM infants.[16]This may be explained by the fact that hyperglycemia in the fetus stimulates insulin, insulin-like growth factors, growth hormone, and other growth factors, which increase fetal development and fat and glycogen deposition. Kurtolu et al. investigated the positive connection between IGF-1 levels and birth weight, cord hemoglobin, and ferritin levels in term healthy newborns.[17]

Hashim et al. demonstrated a significantly significant birth weight difference between IDMs and controls. IDMs had a mean birth weight of 3,841 grammes, whereas controls had a mean birth weight of 3,225 grammes ($p < 0.001$).[18] According to earlier research, the frequency of IDMs with macrosomia is decreasing from sixty percent to between twenty and thirty-five percent, likely due to intensive detection and treatment of diabetes during pregnancy.[19] 5% of fetuses of women with severe diabetic vascular disease are at risk for fetal growth deceleration, defined as birth weight less than the fifth percentile for gestational age; this may be explained by the poor management of diabetes mellitus.[20] In addition, another Japanese research indicated that preterm labour and low birth weight are more likely in diabetes pregnancies.[21]

In the pilot research conducted by MacQueen et al., birth weight had no influence on iron readings regardless of gestational age.[22] The single exception was serum ferritin; increasing gestational age was related with greater serum ferritin levels ($r^2 = 0.25$), but increasing birth weight was associated with lower serum ferritin levels ($r^2 = 0.25$) at any given gestational age.

Cord blood indices in SGA

Among SGA neonates, mean cord hemoglobin was 15.89 ± 1.85 gm/dl, mean cord iron level was 149.19 ± 36.68 mcg/dl, mean cord ferritin was 68.9 ± 23.15 ng/ml and mean TIBC was 318.48 ± 63.71 mcg/dl. We observed that 4.8% had low cord blood hemoglobin, 4.8% had low cord blood iron, 4.8% had low cord blood ferritin and 9.5% had high TIBC.

Kim et al. compared the iron status of newborns born short for gestational age (SGA) and appropriate for gestational age (AGA).[23] The babies with SGA had greater hematocrit levels than those with AGA (50.6% ± 5.8% vs. 47.7% ± 5.8%, P< 0.05). Serum ferritin levels (ng/mL) did not change across groups (mean [95 percent confidence interval]: SGA babies vs. AGA infants, 139.0 [70.0–237.0] vs. 141. SGA newborns exhibited lower ferritin levels after correcting for gestational age (147.1 ng/mL [116.3–178.0 ng/mL] vs. 189.4 ng/mL [178.0–200.8 ng/ mL, P< 0.05) Total body iron reserves were lower in SGA babies than in AGA infants (P< 0.05; 185.6 [153.4–211.7] vs. 202.2 [168.4–241.9] vs. 202.2 [168.4–241.9]).

Saha et al. observed that the iron reserves of term and late preterm SGA newborns were equivalent to those of AGA infants.[24] There was no difference in serum ferritin between AGA and SGA children at birth or 60 days of age median [IQR]: 254.0 [214.3–293.8] vs. 259.7 [217.8–301.5] g/L; p = 0.85 or 147.2 [101.4– 193.0] vs. 155.0 [106.6–203.6] g/L; p = 0.81. SGA babies had a mean hematocrit of

55.5 9.6 against 52.4 5.0 at birth (p = 0.10) and 32.1 4.9 versus 31.6 3.8 at 60 days (p = 0.77).

Mukhopadhyay et al., on the other hand, reported reduced cord ferritin levels in term SGA babies.[25] Kim et al. found that iron accretion might be hindered in late preterm SGA newborns, despite the fact that they did not analyze ferritin levels in these infants. There was no difference in serum ferritin levels between AGA and SGA infants at birth. Kim's research indicates that the SGA group was exposed to the danger of iron shortage due to statistically significant variations in blood ferritin levels after correcting for GA. In addition, the TBI was considerably lower in the SGA groups, indicating that it may be a useful predictor of iron storage impairment in SGA newborns.

Iron deficiency anemia

Based on the hematological criteria of diagnosing iron deficiency anemia (low hemoglobin, low ferritin and high

TIBC), 5 neonates in our sample (6.7%) had iron deficiency anemia.

MacQueen et al. performed a pilot research in which the iron status in the cord blood of a cohort of SGA, IDM, VLBW, and healthy newborns was evaluated. Fifty umbilical cord samples were collected: 20 from healthy comparison neonates between 31 and 40 weeks of gestation, 10 from SGA neonates between 33 and 40 weeks of gestation, 10 from IDM neonates between 36 and 39 weeks of gestation, and 10 from VLBW neonates between 25 and 31 weeks of gestation. In their study, five of the thirty infants in the at-risk groups and one of the twenty infants in the comparison group exhibited a pattern consistent with biochemical iron deficiency; namely, low values (outside the interquartile range of the infants in the comparison group) for serum iron, percent iron binding saturation, and serum ferritin, and high values for soluble transferrin receptor and zinc protoporphyrin to heme ratio. Five of the 30 infants in the at-risk groups and one of the 20 infants in the comparison group exhibited a pattern consistent with biochemical iron deficiency; namely, low values (outside the interquartile range of the comparison infants) for serum iron, percent iron binding saturation, and serum ferritin, as well as high values for soluble transferrin receptor and zinc protoporphyrin to heme ratio.

16 newborns with biochemical iron shortage exhibited low blood iron, poor transferrin saturation, and low serum ferritin levels, according to a follow-up research by MacQueenetal.Two exhibited microcytosis, which is characterized as an MCV below the 5th percentile lowest age reference interval. One of those with microcytosis had a borderline low hemoglobin level for gestational age of 13.7 g/dL.

Maternal age and gravida status with IDA

We observed that iron deficiency anemia in neonate was not significantly associated with maternal age (p value = 0.16). In addition, gravida status of the mother was not significantly associated the iron deficiency anemia (p value = 0.31).

In the research by Morton et al., there was no significant association between maternal age and cord blood ferritin and haemoglobin.[26] In addition, there was no significant connection between parity, assisted pregnancy, and cord blood ferritin and hemoglobin.

Gestational period with IDA

Among the 5 neonates with iron deficiency anemia, one was very preterm, two were early preterm, one was later preterm and one was early term. Gestational period was not significantly associated with iron deficiency anemia (p value = 0.18).

The positive association between serum ferritin and gestational age indicates that fetal iron reserves are directly connected to gestational age, with earlier gestation being associated with lower iron storage. The newborns with the lowest reserves were exceedingly premature.[27]This may be a result of the late transit of iron via the placenta during the third trimester. These findings are comparable to those of another research that found a strong correlation between S. ferritin and gestational age.

In the research by MacQueen et al., gestational age affected serum iron,percent iron binding saturation, serum ferritin, mean corpuscular volume, and zinc protoporphyrin to heme ratio, but not soluble transferrin receptor level. As gestational age grew, the mean corpuscular volume and zinc protoporphyrin to heme ratio tended to decrease (R2 = 0.45 and 0.31, respectively). Serum iron and serum ferritin rose marginally with increasing gestational age (R2 = 0.26 and 0.25).

Over thirty percent of late preterm newborns at six weeks of age had acquired iron deficiency anemia, according to research by Akkermanset al.[28]Many babies who are recognized as iron deficient at birth may develop iron-limited erythropoiesis or iron deficiency anemia before iron supplementation is initiated.

Maternal anemia with IDA

Among the 5 neonates with iron deficiency anemia, mother of only one had anemia. Maternal anemia was not found to be significantly associated with iron deficiency anemia (p value = 0.56).

Kim et al. found no significant association between maternal iron insufficiency and low serum ferritin and total body iron reserves in neonates. In their investigation, SGA newborns with maternal iron insufficiency had median serum ferritin levels of 104 and median total body iron reserves of 180.9.

Akkurt et al. observed that the SGA group had increased maternal ferritin levels.[29] High maternal ferritin may result in hemoconcentration, which reduces uteroplacental blood flow, increases oxidative stress owing to an increase in free iron, and is related to inflammatory responses from placental insufficiency, according to their hypothesis.

Four of the mothers of iron-deficient neonates in a recent research by MacQueen et al showed low biochemical iron indicators, but none developed iron deficiency anaemia. It is doubtful that their newborns had iron deficit based only on maternal iron shortage. In these pregnancies, iron transport through the placenta may have been inhibited, perhaps by hepcidin or another iron transport inhibitor. Ferroportin transports iron from maternal transferrin-bound iron to the fetal blood through transferrin receptors on the placental microvillous membrane surface.[30]Thetransplacental iron transfer in such pregnancies requires more study.

In a recent research, Shukla et al. shown that maternal anemia influences the iron status of exclusively breastfed

full-term babies.[31]Newborns born to anemic moms have considerably lower Hb and ferritin levels than infants born to nonanemic mothers.

Antenatal iron supplementation with IDA

Among the 5 neonates with iron deficiency anemia, all five have maternal history of iron supplementation during the antenatal period (p value = 0.58).

We were unable to locate a research that assessed the relationship between maternal prenatal iron supplementation and iron insufficiency in newborns. Morton et al. found that the median cord blood ferritin content was significantly lower in neonates of women who had three or more servings of milk per day (131 vs. 151 mcg/L, p=0.04). There were associations that were close to significance between maternal consumption of two or more servings of meat, meat substitutes, and eggs per day and lower cord ferritin (102 vs. 145 mcg/L, P=0.06) or Hb (154 vs. 161 g/dL, P=0.09) levels.

Berglund et al. investigated the function of iron supplementation in newborns with BW between 2000 and 2500 g. (mean BW 2.3 kg and gestation 36.5 week).[32] At 6 weeks of age, prior to iron supplementation, the mean serum ferritin concentration was 115–124 g/L, which is within the normal range. Aggarwal D examined the impact of iron supplementation in term, healthy, LBW (2500 g), breastfed babies aged 50–80 days. At around 2 months of age, the serum ferritin levels of their study babies varied from 168.01 to 190.76 g/L, which is again within the normal range.[33]

Risk factor with IDA

We observed that among the 5 neonates with iron deficiency anemia, one was IDM, one was SGA and three were VLBW. We observed that risk factor category was not significantly associated with iron deficiency anemia (p value = 0.28).

Various risk factors, such as SGA and IDM, may have different impacts on the iron status of preterm newbornsvs term infants.[34]MacQueen et al. discovered that serum ferritin rose with gestational age, although birth weight was inversely proportional to serum ferritin at any given gestational age. With greater body mass, it is expected that extra red blood cells are required to boost the oxygen-carrying capability of the bigger tissue area. Polycythemia and large-for-gestational-age may occur in IDM. The more red blood cells formed in this stage need iron, therefore the iron storage forms in these newborns may be diminished.

Sex of new born with IDA

Among the 5 neonates with iron deficiency anemia, three were males and rest two were females. Sex of the new born was not significantly associated with iron deficiency anemia (p value = 0.62).

To the best of our knowledge, we were unable to locate a research that evaluated gender differences in iron deficiency anemia among newborns at risk.

However, there is scant research on gender differences among healthy neonates.

Tamura et al. discovered that the mean cord serum ferritin content of 116 female babies was 43 g/l more than that of 139 male infants. According to Kelly et al, the mean cord ferritin of male babies was higher than that of female infants, although the difference was not statistically significant.[35]It is unknown why these differences may occur. There is a chance that the discrepancy is caused by sex hormones. Male babies may have had higher blood circulation volumes than female fetuses. If the quantity of ferritin generated during gestation is the same for both sexes, male fetuses may experience more ferritin dilution than female fetuses. Third, there may be a greater need for iron to build a bigger quantity of erythrocytes in male fetuses than in female fetuses, resulting in fewer ferritin (body iron storage) in the male circulatory system. Future research is required to validate our results.

CONCLUSION

Based on the results of our study, we conclude that: among IDM, 6.3% had low cord blood hemoglobin, 6.3% had low cord blood iron, 3.1% had low cord blood ferritin and 6.3% had high TIBC.Among VLBW neonates, 9.1% had low cord blood hemoglobin, 18.2% had low cord blood iron, 13.6% had low cord blood ferritin and 18.2% had high TIBC. Among SGA neonates, 4.8% had low cord blood hemoglobin, 4.8% had low cord blood iron, 4.8% had low cord blood ferritin and 9.5% had high TIBC. Iron deficiency anemia was diagnosed in 6.7% of the at-risk neonates. None of the maternal or neonatal factors were significantly associated with iron deficiency anemia.

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