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Umbilical Cord Blood Screening for Congenital Iron Deficiency in Neonates Born by Cesarean Section

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ABSTRACT

Background: A high level of hemoglobin at birth is one of the iron reserves needed by infants to deal with iron deficiency anemia. This study aimed to assess the iron status in neonates born by cesarean section and the effect of maternal characteristics and other laboratory measures on neonatal iron levels. Moreover, it was designed to investigate anemia and identify its factors.

Methods: This descriptive correlational study was conducted in 2022 on 50 neonates by caesarean section in Babylon Hospital, Iraq. Serum ferritin and other laboratory parameters from neonatal umbilical cord blood were measured in addition to others that had been recorded for both neonates and their mothers.

Results: The data were analyzed using the t-test. Out of 50 neonates, 8 infants had low serum ferritin levels and 4 of these 8 had anemia, and 6 of them were born to mothers from rural areas. The mean maternal age of neonates with low serum ferritin was significantly higher than those with normal or high serum ferritin. The results showed that the place of residence and its clean climate and healthy nutrition can have a direct effect on the ferritin level. No significant effect of serum ferritin on WBC, reticulocytes, and platelet counts was observed in this study.

Conclusion: Anemia is significantly associated with low serum ferritin neonates; in addition, maternal age and residence have significant effects on neonatal serum ferritin. Considering the high prevalence of iron deficiency anemia in mothers and even in mothers with proper nutrition, iron deficiency in the mother leads to a decrease in the baby's reserves and makes him susceptible to iron deficiency in the first months after birth. The importance of using iron supplements during pregnancy becomes clearer, and one should not be satisfied only with diet. Due to the adverse effects of increasing the number of pregnancies on the mother's iron reserves, appropriate spacing should be observed.

Keywords: Cesarean, Ferritin, Iron deficiency anemia, Neonates, Umbilical cord blood

Introduction

Iron is considered one of the nutritionally essential trace elements in the human body, and it acts through incorporation into various proteins and enzymes. Moreover, iron is available in the diet in ferric and ferrous forms. Ferrous iron is directly absorbed across the brush border enterocytes (mostly duodenum and upper jejunum enterocytes) by divalent metal ion transporter 1. Ferric iron cannot be absorbed unless converted to ferrous form in the presence of an iron reductase enzyme. Absorbed iron will be transferred across the mucosa to the blood (1).

After entering blood, iron will bind to transferrin to be transported to cells and bone marrow for erythropoiesis (2). In the body, most iron exists intracellularly, as ferritin in the cytosol, and hemosiderin, which represents a very small portion of body iron stores and comes from the breakdown of ferritin within lysosomes mostly in macrophages (3). Iron deficiency occurs when

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there are decrements in iron supply to tissues and bone marrow (4). Iron deficiency could occur with or without anemia (5) causing defects in cognitive development and immunity mechanisms (6, 7). Additionally, deficiencies in iron levels during pregnancy resulted in various adverse outcomes for both mother and infant, such as a higher risk of sepsis, maternal mortality, perinatal mortality, and low birth weight. Furthermore, iron deficiency and anemia limit learning ability and elevate morbidity rate (8).

Regarding neonates, iron deficiency could be associated with long-term neurocognitive problems (9) as shown in experimental studies (10-12). In case of iron deficiency anemia, further iron supplementation will correct the anemia but not iron deficiency in brain tissues (10-12) as shown in animal models when it had been noted that iron is preferentially shifted for erythropoiesis rather than brain accretion (13).

In neonatal infants, the development of iron deficiency depends on certain risk factors; these factors include [1] small-for-gestational-age neonates (SGA), [2] infants of diabetic mothers (IDM), and [3] very low birth weight (VLBW) preterm neonates (14, 15). Low birth weight (LBW) is defined as any live birth weighing less than 2500-gram, while VLBW is categorized as weights below 1500-gram and both LBW and VLBW infants are mostly preterm (16) (preterm infants are those who are born before 37 weeks from the first day of the last menstrual period) (17).

These three groups are also at higher risk of developing neurocognitive defects. In general, serum iron levels of neonates born to women who had iron deficiency anemia during pregnancy were comparable to those born to iron-replete women; however, the serum ferritin levels in the former were lower indicating low iron stores (18). It has been suggested that under normal conditions, fetal iron levels are regulated by compensatory mechanisms that protect infants from iron deficiency anemia at birth (19, 20). This protection, however, might not be sufficient to counteract neurocognitive delay, and this is because of some pathological conditions that compromise maternal iron transport to the fetus (18-21).

Iron deficiency observed in infants born small for gestational age or those born to diabetic mothers might be related to such pathological conditions. Adding to that, preterm infants do not have the advantage of large iron mass that usually occurs in the third trimester of pregnancy making them vulnerable to developing iron deficiency anemia at birth (18-22). Depending on the severity, iron deficiency can be categorized into three groups (23). First, iron deficiency with normal erythropoiesis characterized by low serum ferritin and low serum iron. Second, iron deficiency with iron-limited erythropoiesis recognized by the reduction in both reticulocyte-hemoglobin content and mean capsular volume (24, 25), without decrement in hemoglobin or hematocrit (without anemia) (23, 26). The third group, which is next degree in severity, is iron deficiency with iron deficiency anemia that is diagnosed by reduced hemoglobin and hematocrit values (23). In the present study, in addition to investigating the prevalence of iron deficiency and the resulting anemia in pregnant mothers, its relationship and effects on the iron status of the neonates have also been evaluated. Accordingly, the main objective is to check the amount of iron in the blood.

Methods

This descriptive correlational study was conducted at Babylon Hospital for Pediatric and Gynecology. In total, 50 newborn infants who had been delivered by cesarean section were enrolled in this study. In order to perform the tests, with the permission of the parents and according to the ethical rules of the hospital, 50 babies were examined, of which 53% were boys and 47% were girls. The weights of the babies were between 1400 and 4750 grams with an average of 2.33±0.59 grams. All pregnancies were on time and without complications. Mothers with abnormal bleeding, placental abruption, placenta previa, diabetes, pre-eclampsia, anemia, premature, and late-term cases, as well as babies with genetic diseases, were excluded from the study. The time of closing the umbilical cord in all cases was immediately after birth (up to 15 seconds). One cc of blood was taken from the umbilical vein to measure hemoglobin and hematocrit after birth and stored in a tube containing Ethylenediaminetetraacetic acid anticoagulant. All samples were sent to a laboratory.

A previously arranged checklist sheet was used to obtain sociodemographic data, such as gestational age, gender and birth weight, maternal age, and residence, in addition to maternal clinical data, including parity, spacing, as well as presence and type of maternal disease (anemia, diabetes mellitus, and hypertension). Regarding neonatal laboratory parameters, three-ml blood samples were drawn from the neonates' clamped umbilical cords for the measurement of serum ferritin levels, packed cells volume (PCV), white blood cells (WBC) count, platelet count, and reticulocyte count. The results were recorded, and at the end of the study, the recorded data were computer-aided using SPSS software (version 27) for statistical analysis. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (means±SD). Student t-test was used to compare means between the two groups. Fisher's Exact Test was utilized to find the association between categorical variables. A *P*-value of ≤0.05 was considered statistically significant.

Ethical approval

This study and its protocol were approved by the authority of the health institution at Babylon Hospital (Code: BHJ., EC: 12-3-2022, 233). Also, we applied the American Psychological Association's ethical principles. The involved applicants (or their relatives) provided a written informed agreement. The whole research was conducted according to the Helsinki Declaration.

Results

The study was carried out in Babylon Hospital for Pediatric and Gynecology. A total of 50 umbilical cord blood samples were collected from 50 newborn babies delivered by cesarean section. The mean gestational age was 35.46±2.25 weeks with a maximum gestational age of 40.00 weeks and a minimum gestational age of 30.00 weeks. It should be mentioned that the majority of newborn babies were preterm (n=35, 70.0%). The mean birth weight was 2.33±0.59 kg with a maximum birth weight of 4.75 kg and a minimum birth weight of 1.40 kg. Moreover, the majority of newborn babies presented with LBW (n=34, 68.0%). It is worth mentioning that the majority of newborn babies were male (n=33, 66.0%) as shown in Table 1.

Table 1. The distribution of newborn babies according to sociodemographic characteristics (n=50)

Sociodemographic characteristics	Number	%
Gestational age		
Term baby (≥ 37 weeks)	15	30.0%
Preterm (<37 weeks)	35	70.0%
Total	50	100.0%
Gender		
Male	33	66.0%
Female	17	34.0%
Total	50	100.0%
Birth weight		
Low birth weight	34	68.0%
Normal birth weight	15	30.0%
Large for gestational age	1	2.0%
Total	50	100.0%

*Mean gestational age was 35.46±2.25 weeks with a maximum gestational age of 40.00 weeks and a minimum gestational age of 30.00 weeks. The mean birth weight was 2.33±0.59 kg with a maximum birth weight of 4.75 kg and a minimum birth weight of 1.40 kg

Concerning maternal characteristics, the mean maternal age was 28.84±7.73 years; in addition, the youngest mother was 17 years old, while the oldest mother was 43 years old. The mean duration between pregnancies was 26.46±17.90 months with a minimum spacing of 5 months and a maximum spacing of 84 months. The majority of mothers came from rural area (n=33, 66.0%) and most of them (n=21, 42.0%) presented with P3-P4. Furthermore, 13 (26.0%) mothers represent maternal diseases as shown in Table 2.

Depending on ferritin level values, the patients were grouped into three categories depending on the normal range of ferritin levels (27), including low<25 ng/ml, normal 25-200 ng/ml, and high>200 ng/ml. Low serum ferritin represents 8 (16.0%) newborn babies. Normal serum ferritin represents 37 (74.0%) newborn babies, and babies with high serum ferritin represent 10.0% (n=5) of the study sample as shown in Figure 1.

Afterward, the association between sociodemographic characteristics of newborn babies (e.g., gestational age, gender, and birth weight) and serum ferritin level (low<25 ng/ml and normal/high≥25 ng/ml) was investigated using

Table 2. The distribution of newborn babies according to maternal characteristics (n=50)

Maternal characteristics		
Maternal age (years)	(28.84±7.73)	(17-43)
Residence		
Rural	33	66.0%
Urban	17	34.0%
Total	50	100.0%
Parity		
P0	8	16.0%
P1-P2	15	30.0%
P3-P4	21	42.0%
P5-P6	6	12.0%
Total	50	100.0%
Spacing		
< 2 years	22	44.0%
≥ 2 years	28	56.0%
Total	50	100.0%
Maternal disease		
Yes	13	26.0%
No	37	74.0%
Total	50	100.0%
Type of maternal disease		
Anemia (receive blood)	6	46.2%
Diabetes mellitus	5	38.4%
Hypertension	2	15.4%
Total	13	100.0%

*Mean spacing time was 26.46±17.90 months with maximum spacing of 43.00 months and minimum spacing of 17.00 months.

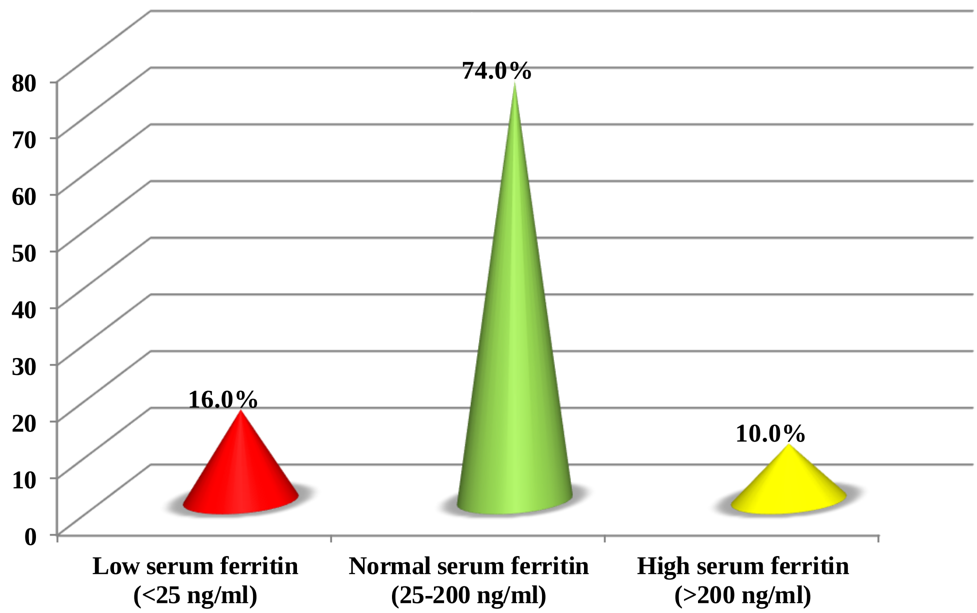

Figure 1. Distribution of newborn babies according to serum ferritin level

Fisher's Exact Test. There was no significant association between sociodemographic characteristics and serum ferritin level as shown in Table 3.

When the mean maternal age of the low serum ferritin group was compared with that of normal or high ferritin level groups, it was noticed that the former was significantly higher than the latter's as shown in Table 4 and Figure 2.

Regarding the relationship of maternal characteristics (residence, parity, spacing, and maternal diseases) with neonatal ferritin levels, table 5 shows the association between maternal characteristics and serum ferritin levels (e.g., low<25 ng/ml and normal/high≥25 ng/ml). There was a significant association between maternal residence and serum ferritin level.

The normal range of PCV is 45%-65% ng/ml (28). Figure 3 shows the association between PCV (%) (anemia <45% and normal PCV 45%-65%) and serum ferritin level (low<25 ng/ml and

Table 3. The association between sociodemographic characteristics and serum ferritin level (n=50)

Sociodemographic characteristics	Serum ferritin level		Total	P-value
	Low (<25 ng/ml)	Normal or high (≥ 25 ng/ml)		
Gestational age (weeks)				
Term baby (≥ 37 weeks)	4 (50.0)	11 (26.2)	15 (30.0)	0.22
Preterm (<37 weeks)	4 (50.0)	31 (73.8)	35 (70.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	
Gender				
Male	7 (87.5)	26 (61.9)	33 (66.0)	0.237
Female	1 (12.5)	16 (38.1)	17 (34.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	
Birth weight				
Low birth weight	6 (75.0)	28 (66.7)	34 (68.0)	1.000
Normal birth weight	2 (25.0)	13 (31.0)	15 (30.0)	
Large for gestational age	0 (0.0)	1 (2.3)	1 (2.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	

*P-value ≤ 0.05 was significant. Fisher's Exact Test.

Table 4. The mean differences of maternal age according to serum ferritin level (n=50)

Study variable	Serum ferritin level	N	Mean±SD	t-test	*P*-value
Maternal age (years)	Low (<25 ng/ml)	8	35.63±8.42	2.909	0.005*
	Normal or high (≥ 25 ng/ml)	42	27.55±6.97		

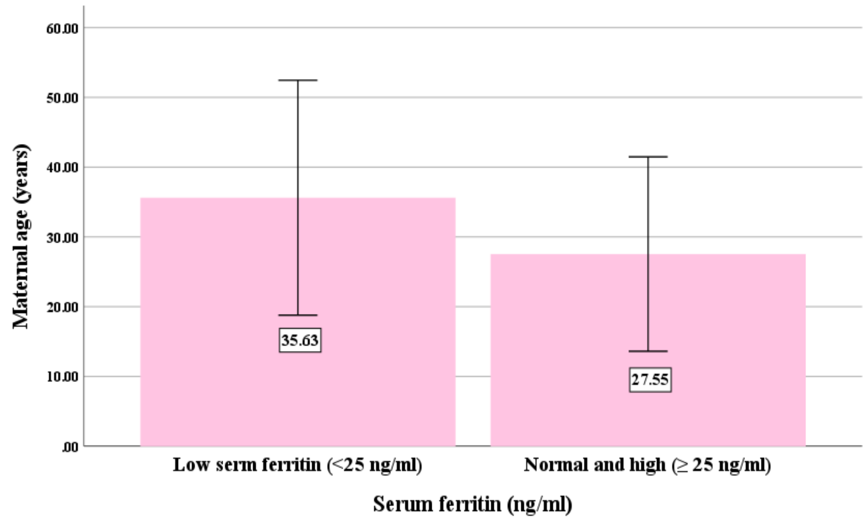

Figure 2. The mean differences of maternal age (years) according to serum ferritin level

normal/high≥25 ng/ml). There was a significant association between PCV (%) and serum ferritin level. From those with low serum ferritin, 4 (50.0%) neonates presented with anemia PCV <45%, from those neonates with normal or high serum ferritin, 6 (14.3%) neonates presented with anemia PCV <45%.

Regarding differences between serum ferritin

Table 5. The association between maternal characteristics and serum ferritin level (n=50)

Maternal Characteristics	Serum ferritin level		Total	P-value
	Low (<25 ng/ml)	Normal or high (≥ 25 ng/ml)		
Residence				
Urban	6 (75.0)	11 (26.2)	17 (34.0)	0.013*
Rural	2 (25.0)	31 (73.8)	33 (66.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	
Parity				
P0	0 (0.0)	8 (19.0)	8 (16.0)	0.389
P1-P2	3 (37.5)	12 (28.6)	15 (30.0)	
P3-P4	5 (62.5)	16 (38.1)	21 (42.0)	
P5-P6	0 (0.0)	6 (14.3)	6 (12.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	
Spacing				
< 2 years	2 (25.0)	20 (47.6)	22 (44.0)	0.439
≥ 2 years	6 (75.0)	22 (52.4)	28 (56.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	
Maternal diseases				
Yes	4 (50.0)	9 (21.4)	13 (26.0)	0.181
No	4 (50.0)	33 (78.6)	37 (74.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	

**P*-value ≤ 0.05 was significant. Fisher's Exact Test.

Table 6. The mean differences of study variables according to serum ferritin level (n=50)

Study variable	Serum ferritin level	N	Mean±SD	t-test	P-value
WBC count (10^9/L)	Low (<25 ng/ml)	8	12.40±3.45	-0.645	0.522
	Normal or high (≥ 25 ng/ml)	42	13.32±3.74		
Platelet count (10^9/L)	Low (<25 ng/ml)	8	249.13±63.49	0.504	0.616
	Normal or high (≥ 25 ng/ml)	42	228.31±112.80		
Reticulocyte count (%)	Low (<25 ng/ml)	8	5.75±1.58	-0.602	0.55
	Normal or high (≥ 25 ng/ml)	42	6.48±3.32		

levels (low <25 ng/ml and normal/high ≥ 25 ng/ml) and other laboratory variables (WBC count, platelet count, and reticulocyte count), table 6 showed no significant differences among the means of study variables according to serum ferritin level.

Discussion

Ferritin levels of the neonates were classified into three groups, namely low, normal, and high. Results showed that 74% of cases were normal which was in agreement with the findings of previous studies (11, 23). Moreover, it was found that maternal age significantly affected the ferritin level of the neonates, as the mother's age increases to over 35, the number of neonates with low ferritin levels increases. The results showed that the place of residence and its clean climate and healthy nutrition can have a direct effect on the ferritin level, which is in agreement with (29). Serum ferritin concentration represents a standard measure for the body's iron stores (29). At the beginning of this century, several assumptions led to the development of the idea that iron deficiency at birth is very rare if not almost non-existent (9-12). Many reasons led to these assumptions, such as the observation that low maternal iron levels did not lead to iron deficiency in their born neonates (18, 19). Furthermore, the fetus will excellently search for and gain its iron needs from maternal iron independent of her iron levels (30), and whether the mother is receiving iron supplementation during pregnancy or not, will not affect the fetal iron levels (31). However, subsequent assumptions about the possibility of the presence of iron deficiency in neonates have arisen mostly in VLBW premature neonates, SGA infants, and IDM infants (14,15).

In the current study, there is a significant association between low PCV and low ferritin levels as 4 neonates out of 8 with low ferritin levels had low PCV values, while only 6 neonates out of 42 with normal or high ferritin levels had low PCV values. Macqueen et al. (2017) showed that 8 out of 50 studied neonates had iron deficiency but none of them had anemia (32).

Regarding maternal characteristics, there is a significant association between ferritin levels and maternal residence as mothers of 6 iron-deficient neonates came from urban areas, while only the mothers of 2 iron-deficient neonates were from rural areas. The available explanation of this is that rural mothers might have a more healthy diet as consuming vegetables and fruits much more than urban mothers. Teruneh et al. (33) noticed that anemia was more prevalent in babies born to mothers who did not consume vegetables and fruits.

The mean maternal age of iron-deficient neonates was significantly higher than that of neonates with normal or high iron levels. No previous studies correlating maternal age and neonatal iron levels are available. Moreover, no significant effect of serum ferritin was observed on WBC, reticulocytes, and platelet counts.

Conclusion

Iron deficiency anemia is the most common type of anemia in pregnant mothers in the world, which can lead to premature birth and increased maternal and child mortality. Therefore, the investigation of the serum iron status of pregnant mothers and its relationship with the iron status of newborns plays an important role in deciding how to use iron supplements during pregnancy. In this study, we conclude that anemia is more significantly associated with iron-deficient neonates than neonates with normal or high iron levels. Further studies are needed to correlate the effect of maternal residence on neonatal iron levels and whether this effect is attributed to diet quality differences between urban and rural areas or other factors are available. The average of iron-deficient neonates' mothers was significantly higher than non-iron-deficient neonates' mothers. However further studies are needed to understand how the mother's age affects neonatal iron level.

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Not Applied

Conflicts of interest

Authors declare there is no conflict of interests.

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