Original Research Article

Serum Ferritin – The Role of Birthweight

Abstract

Aims: To determine the serum ferritin levels amongst low birth weight neonates and to correlate it with different categories of low birth weight. To determine the role of birth weight in predicting changes in serum ferritin levels.
Methodology: This was a prospective comparative cross-sectional study which was carried out at the Neonatal Intensive Care Unit of the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria between June and December 2014. The study included 140 newborns of all birth weights delivered at the UNTH. These were categorized into extremely low birth weight (ELBW), very low birth weight (VLBW), low birth weight (LBW) normal birth weight and macrosomic. Babies with C-reactive protein levels > 10mg/dl, who were intra-uterine growth restricted, and whose mothers had conditions associated with low iron stores were excluded from the study. Anthropometric measurements were done for all subjects. Serum ferritin was measured at birth and this was correlated with birth weight and gestational age.
Results: Serum ferritin levels ranged from 20.6 to 296.4µg/l. Ferritin levels showed a steady increase in relation to birth weight. (F = 42.453, $P < .001$). There was a significant association between ferritin levels and categories of birth weight. ELBW babies were 98 times more likely to have low ferritin levels than babies with normal weight ($P < .001$, OR = 97.600, 95% C.I = 10.083 – 944.711). VLBW and LBW babies were less likely to have low ferritin levels than babies with normal weight ($P < .001$, OR = 0.070, 95% C.I = 0.017 – 0.291)($P = .006$, OR = 0.201, 95% C.I = 0.064 – 0.635). Only birthweight was a significant positive predictor of low ferritin levels ($P = .024$).
Conclusion: Serum ferritin in new-borns showed a significant association with birth weight. Birth weight is a positive predictor of low serum ferritin levels. [check statements in red and reflect upon them]

Keywords
Birth weight, Ferritin, Iron, Prediction

Introduction

Iron is an important nutrient required for body growth and development [1]. It plays a crucial role in cellular metabolism, enzyme reactions, growth and repair of tissues, and in the development of the immune system [1-4]. Although iron is required for general body growth and development [5-8], it plays a particularly important role in the brain [9-11]. Specific brain development processes that require iron include myelination [12], dopamine (a monoamine) metabolism [12,13], energy metabolism and hippocampal dendritic growth [10,14]. This requirement for iron is of particular importance during the period of rapid brain growth [15]. Iron deficiency (regarded as serum ferritin level <35µg/l) at this stage of development causes significant neurocognitive impairments, which cannot be reversed even with subsequent iron therapy [2,13,16,17].

Risk factors for iron deficiency at birth include; low birth weight; prematurity; maternal illnesses such as diabetes mellitus and hypertension; and maternal lifestyle such as smoking [18]. In utero, iron accretion occurs trans-placentally starting from 24 weeks of gestation and becoming maximal in the third trimester,

when rates reach 1.35mg/kg [2]. This period of maximum accretion also coincides with the period of maximum foetal weight gain, with a corresponding average iron content of 75 mg/kg of body weight in the third trimester [2]. Studies have also shown that, foetal weight gain increases steadily during this period, reaching up to 24-25g/day in the third trimester [19]. With this daily increase in body weight, there is an attendant increase in blood volume and organ mass, and thus an increased requirement and capacity for iron storage [20]. However, even though a close interplay exists between in utero acquisition of weight and advancement in gestational age, certain conditions may give rise to a discordance between the two resulting in varying degrees of growth restriction despite advancement in gestational age [21,22]. These conditions result from a reduction in trans-placental transfer of nutrients, including iron, needed for normal growth [21].

Clinical signs of iron deficiency amongst neonates include paleness, reduced activity, feeding intolerance, edema, and an increased heart and respiration rate [2,23]. These are however late signs which do not occur until there is depletion of the brain's iron stores [2]. Therefore, identifying neonates who are at risk of low iron stores is critical in improving long term neurological outcomes. Several studies have established the relationship between iron stores and gestational age [20,24-30]. Literature on its relationship with birth weight +-are however few. We postulated that the serum ferritin levels increase with increasing birth weight. We also postulated that the increase in ferritin levels which occur during gestation is a factor of weight gain rather than only duration of gestation. This study thus aimed to determine the serum ferritin levels amongst low birth weight neonates and to correlate it with different categories of low birth weight. The study also aimed at determining the role of birth weight in predicting changes in serum ferritin levels.

Materials and Methods

This prospective comparative cross sectional study was carried out at the Neonatal Intensive Care Unit of the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria between June and December, 2014. The study included 140 neonates of all birth weights. These were categorized as follows: extremely low birth weight (<1000g); very low birth weight (1000g - <1500g); low birth weight (1500g - <2500g); normal birth weight (2500g - <3500g); and macrosomic (3500g and above). Babies with C-reactive protein levels > 10mg/dl, who were intra-uterine growth restricted, and whose mothers: had ante partum haemorrhage or other bleeding episodes during pregnancy; had severe anaemia (haemoglobin cut-off point of less than 11g/dl defines maternal anaemia in the later stages of pregnancy [31]); diabetes mellitus or hypertension; and who smoked were excluded from the study. Subjects were enrolled consecutively until the calculated sample size was reached. The study was approved by the University of Nigeria Teaching Hospital Health Research Ethics Committee. Written informed consent was obtained from the parents of the study participants.

Data was collated and analysed using Statistical Package for Social Sciences (SPSS) Version 20. Relationships between continuous variables were determined using correlation and linear regression analysis. Means of continuous variables were compared using Student's t-test, while associations between categorical variables were determined using chi-square and logistic regression analysis as applicable. All tests were considered significant at $P < .05$.

Blood Sample Collection

Umbilical venous blood was collected from a double clamped segment of the umbilical cord during delivery. This was then placed into a small study designated storage box at room temperature designated. Subsequently, the Howard Kelly forceps on one end of the section of the cord was removed. The umbilical vein was identified and depending on its size, a 5,6 or 8 Fr gauge nasogastric tube attached to a 10ml syringe was inserted and at least 6ml of blood was withdrawn. Where this did not work, the blood was obtained by venopuncture of the side of the cord corresponding to the identified umbilical vein. A

drop (approximately 0.2 ml) of the blood obtained was first immediately dropped onto a microcuvette which was inserted into the Hemocue® Hb 201^{+} for estimation of haemoglobin concentration. Serum was then obtained from the remaining blood for both CRP and ferritin estimation at the Haematology laboratory of UNTH using the Diagnostic Automation 800 ELISA machine®. Low ferritin was regarded as a measured serum level of less than 35µg/l [20].

Sample Size Determination

The sample size (n) for an infinite population of more than 10,000 was first obtained using the formula for the comparison of proportions [32]:

$$n = \frac{[P1(1 - P1) + P2(1 - P2)]}{(P1 - P2)^2} \times \text{Cp power}$$

Where:
P1 = Proportion of preterm babies from a previous study(10%) [28]
P2 = Proportion of term babies from a previous study (18%) [28]
Cp power = 13 when p value is 0.05 and power is 95%
Therefore:

$$n = \frac{[(0.1)(0.9) + (0.18)(0.82)]}{(-0.08)^2} \times 13 = 483$$

Since this study was done on a finite population (less than 10,000), the sample size for a finite population was then derived using the formula below [33].

$$nf = \frac{no}{(1 + no/N)}$$

Where :
nf = final (or minimum) sample size
no = initial sample size (derived above)
N = population of preterm births over a 12 month period in UNTH i.e. 70.

$$nf = \frac{483}{(1 + 483/70)} = 61$$

An attrition rate of 10% was used in the study to account for possible sample loss. Thus, the total minimum sample size was calculated to be 67 preterm babies, which was rounded off to 70 each.

Results

Study characteristics

The baseline characteristics of the study population is shown in Table I. There were 68 males and 72 females, giving a male to female ratio of 0.9:1. Mothers of 84 (60%) babies reside in urban areas while mothers of 56 (40%) babies reside in rural areas. Majority of the subjects (36.4%) were of the upper socioeconomic class.

Table I: Demographic, maternal and neonatal variables

Characteristics	Preterm n = 70 (50%)	Term n = 70 (50%)	Total n = 140 (100%)
Gender			
Male	34 (24.3)	34 (24.3)	68
Female	36 (25.7)	36 (25.7)	72
	70	**70**	**140**
Tribe			
Ibo	68	64	132
Yoruba	1	3	4
Hausa/Fulani	1	3	4
	70	**70**	**140**
Socioeconomic Class			
Upper	27	24	51
Middle	15	26	41
Lower	28	20	48
	70	**70**	**140**

The gestational age of the study population ranged from 25 weeks to 39 weeks, with birth weight ranging from 0.55kg to 5.2kg. The distribution of other anthropometric parameters amongst the study population is shown in Table II.

Table II: Anthropometric indices of the study population

Weight categories (g)	N	OFC (cm)	CC (cm)	Length (cm)

	(140)	Mean (SD)	Mean (SD)	Mean (SD)
<1000g (ELBW)	9	24.17 (1.44)	21.44 (1.74)	26.44 (6.31)
1000-<1500g (VLBW)	13	30.35 (1.34)	28.73 (2.48)	39.54 (4.68)
1500g-<2500g (LBW)	38	31.19 (7.34)	30.83(2.94)	43.07 (3.83)
2500 - <3500 (Normal)	66	34.96 (4.37)	33.82 (2.25)	48.02 (2.14)
≥3500 (Macrosomia)	14	37.12 (1.02)	36.61(1.65)	52.93 (2.64)
TOTAL	**140**	**33.03 (5.81)**	**32.02 (4.23)**	**44.99 (6.90)**

Ferritin levels in the study population

Serum ferritin levels ranged from 20.6 to 296µg/l with a mean of 93.1µg/l ± 57.7. Low serum ferritin was observed in 22% of the population. Ferritin levels showed a steady increase in relation to birth weight. (F = 42.453, *P* < .001) (Table III). However, this difference was not significant between ELBW and VLBW babies.

Table III: Comparison of mean ferritin levels by birthweight

	Birthweight						
	*ELBW	*VLBW	LBW	Normal	Macrosomia	F	*P* value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
Ferritin levels	29.79 ± 5.55	42.96 ± 13.94	64.13 ± 33.67	106.82 ± 46.00	194.76 ± 41.89	42.453	< .001

**Duncan multiple comparison indicating means not significantly different*

There was an inverse relationship between the prevalence of low serum ferritin and birth weight, with significantly higher prevalence occurring in the ELBWT, VLBWT and LBWT categories, when compared with normal birth weight babies. There was also a significant association between ferritin levels and categories of birth weight (P = .05) (Table IV). ELBWT babies were 98 times more likely to have low ferritin levels than babies with normal weight (P < .001, OR = 97.600, 95% C.I = 10.083 – 944.711). VLBWT babies were less likely to have low ferritin levels than babies with normal weight (P < .001, OR = 0.070, 95% C.I = 0.017 – 0.291). Similarly, LBWT babies were less likely to have low ferritin levels than babies with normal weight (P = .006, OR = 0.201, 95% C.I = 0.064 – 0.635). All the macrosomia babies have normal ferritin levels. [cross check these statements carefully with the documented results please]

Table IV: Association between ferritin levels and categories of birth weight

	Ferritin levels		*P* value	OR	95% C.I for OR
	Low	Normal			
Birth weight (kg)	n (%)	n (%)			
Normal	5 (7.6)	61 (92.4)			
ELBWT	8 (88.9)	1 (11.1)	< .001	97.600	10.083 – 944.711
VLBWT	7 (53.8)	6 (46.2)	< .001	0.070	0.017 – 0.291
LBWT	11 (28.9)	27 (71.1)	.006	0.201	0.064 – 0.635
Macrosomia	0 (0.0)	14 (100.0)	NA	NA	NA

**NA = Not applicable*

Prediction of low ferritin

After including birthweight and GA in a multivariate logistic regression model, only birthweight was a significant positive predictor of low ferritin levels (P = .024). Analysis also showed that a unit decrease in birth weight led to a five times increased likelihood of having low serum ferritin levels (OR = 4.58, 95%

C.I = 1.223 – 17.149). There was no significant risk of having low ferritin levels with reducing gestational age (Tables V and VI).

Table V: A multivariate logistic regression of Birthweight and GA predicting low ferritin levels

	P value	OR	95% C.I for OR
Birthweight	.024	4.580	1.223 – 17.149
GA	.599	1.085	0.801 – 1.468

Table VI: A multivariate analysis of the predictors of ferritin levels

	R	R^2	B	*P* value
Birthweight	0.756	0.571	40.862	< .001
GA			0.288	.875

Discussion

In this prospective study, serum ferritin was used to assess iron stores in both preterm and term babies with a birth weight below normal. Several other markers are available to assess total body iron and iron stores [34-41]. Some of these include serum iron, haemoglobin (Hb) and ferritin concentrations [35-37], mean corpuscular volume (MCV) [11], total iron binding capacity [34], transferrin saturation [34], red cell distribution width [34], zinc protoporphyrin [37], and serum transferrin receptor (sTfR) [39-41]. However, each of these has major limitations, some of which include a lack of association with gestational age [39,41], and a lack of specificity for iron deficiency [11,34]. Serum ferritin levels are reduced only in iron deficiency [11,20], with a serum ferritin level less than 35µg/l being the cut-off in newborn babies [18]. On the other hand, serum ferritin levels are elevated during infection, inflammation and neoplasia [11,20]. Under these conditions, its elevated levels can mask the diagnosis of iron deficiency [11,20].

In this study, serum ferritin levels of new-born babies showed a steady rise with increasing birth weight. This finding in both preterm and term low birth weight babies is consistent with the reports of several other studies [42-44]. Agarwal and colleagues [43] observed that marginally LBW and LBW had lower serum ferritin levels than normal birth weight babies. This difference however, was not as significant as that obtained in this study, likely as a result of the higher mean gestational age of 36weeks for infants enrolled in their study.

Serum ferritin showed a positive correlation with birth weight, with 57% of the changes that occur in serum ferritin being attributable to birth weight. A similar positive correlation has been observed in some

other European studies [18, 44-58]. Faldella *et* al [45] noted that the smaller the preterm infants are at birth, the more susceptible they are to iron deficiency. In addition, while studying venous and arterial hematologic profiles of very low birth weight infants in Germany, Obladen [46] and co-workers retrospectively reviewed four prospective longitudinal cohort studies. The data sets comprised 562 term and preterm, very low birth weight (VLBW) infants from 20 centres between April 1989 and November 1995 [46]. The authors observed that one quarter of infants had serum ferritin less than 80µg/l and transferrin saturation less than 10% [46], lower than that reported by Arad *et al* [47] and Olivares *et al* [48] in normal birth weight preterm infants [46]. This large proportion in the latter studies may be attributed to the high cut off value (<80µg/l) used to define low serum ferritin. Foetal iron deposit is related to size at birth and to gestational age [18,20]. It has been documented that the average iron content at birth is approximately 75 mg/kg of body weight, with storage occurring mostly during the third trimester of gestation [9,18]. Ferritin represents the storage form of iron, and its serum levels are the standard for the assessment of body iron stores even in preterm babies [20].

This study showed that birth weight was a better predictor of low ferritin levels than gestational age. There is however a dearth of literature from which comparisons can be made. Contrary to the findings of this study, various researchers have reported that preterm birth is a cause of low iron stores, with ferritin levels being lower with decreasing gestational age [20,24-30] Rao and colleagues [19] studied iron in foetal and neonatal nutrition. The authors showed that preterm birth deprives the foetus of the significant iron accretion that occurs beyond 32 weeks gestation [18]. However, the findings of the study also revealed that 25-85% of preterm infants with a birth weight less than 1500g were at risk of iron deficiency during infancy [18]. Thus, this observation may have been attributable to weight rather than gestational age. Sidappa and colleagues [20] also carried out a meta-analysis of 35 published studies over a period of 25 years. They documented a steady increase in ferritin level from a mean of 63µg/l at 23 weeks to 171µg/l at 41 weeks gestation [20]. This analysis and other literature, unlike this current study, did not assess the role of birth weight, independent of gestational age or in its comparison, in determining low serum ferritin levels.

Conclusion

There is a wide variation in serum ferritin levels amongst low birth weight babies. Low serum ferritin levels are also quite prevalent amongst this population with a significant association with categories of birth weight. Birth weight can also positively predict variations in serum ferritin levels in new-born babies

Consent

Written informed consent was obtained from the parents of the study participants.

Ethical Approval

The study was approved by the University of Nigeria Teaching Hospital Health Research Ethics Committee.

Source of funding – Declare the source of funding for the research project.

Conflict of interest – Document if there was or there was no conflict of interest.

Declare the role of each research worker.

References

Preer Gl, Philipp BL. Understanding and managing breast milk jaundice. Arch Dis Child Fetal Neonatal Ed. 2011;96:F461-66. doi: 10.1136/adc.2010.184416. [There is no reference number attached to this reference why and which number do you want to attach to the reference?] YOU NEED TO ENSURE THE REFERENCE NUMBERS ARE WRITTEN WELL AND ALL REFERENCES NUMBERED CORRECTLY IN THE TEXT AND REFERENCE SECTION

1. Leone T, Finer N. Fetal adaptation at birth. Curr Paediatr. 2006; 16: 373 – 378.
2. Siddappa AM, Rao R, Long JD, Widness JA, Georgieff MK. The assessment of newborn iron stores at birth: a review of the literature and standards for ferritin concentrations. Neonatology. 2007;92(2):73-82. doi: 10.1159/000100805. Epub 2007 Mar 14. PMID: 17361090; PMCID: PMC2863301.
3. Cheng C, Juul S. Iron balance in the neonate. Neoreviews. 2011; 12: 148-158.
4. Rosenthal MD, Glew RH. Medical biochemistry: Human metabolism in health and disease. New York (NY): John Wiley & Sons; 2009. p. 372-5.
5. Duncan H. Physiology of fetal adaptation at birth. Curr Paediatr. 1999; 9: 118 - 122.
6. Platt M, Deshpande S. Metabolic adaptations at birth. Semin Fetal Neonatal Med. 2005; 10: 341 – 350.
7. Petty J. Fact Sheet: Normal postnatal adaptation to extrauterine life –Thermoregulation and glucose homeostasis. J Neonat Nurs. 2010; 16: 198-199.
8. Mercer J, Debra A, Owens E, Graves B, Haley M. Evidence based practices for the fetal to neonatal transition. J Midw and Womens Heallth. 2007; 52: 262 – 272.
9. Shao J, Rao R, Georgiff MK, Kaciroti N, Felt BT, Zhao Z, et al. Maternal serum ferritin concentration is positively associated with newborn iron stores in women with low ferritin status in late pregnancy. Nutr. 2012; 142: 2004-2009. Shao J, Lou J, Rao R, Georgieff MK, Kaciroti N, Felt BT, Zhao ZY, Lozoff B. Maternal serum ferritin concentration is positively associated with newborn iron stores in women with low ferritin status in late pregnancy. J Nutr. 2012 Nov;142(11):2004-9. doi: 10.3945/jn.112.162362. Epub 2012 Sep 26. PMID: 23014493; PMCID: PMC3498973. https://pubmed.ncbi.nlm.nih.gov/23014493/ [References 9 and 16 have been repeated and the authors need to effect the changes so that what is now reference16 becomes reference 9 and reference 16 becomes reference 16 and the remaining numbers altered in the text and in the referencing section please]
10. Georgieff MK. The role of iron in neurodevelopment: Fetal iron deficiency and the developing hippocampus.Biochem Soc Trans. 2008; 36: 1267-1271
11. Cheng C, Juul S. Iron balance in the neonate. Neoreviews 2011; 12: 148-158.
12. Lozoff B. Early iron deficiency has brain and behavior effects consistent with dopaminergic dysfunction. J. Nutr. 2011; 141: 740-746.
13. Siddappa AM, Georgieff MK, Wewerkas S, Worwa C, Nelson CA, deRegnier RA. Auditory recognition memory in iron-deficient infants of diabetic mothers. Paed Research. 2004; 55: 1034 – 1045.
14. Georgieff MK, Innis SM. Controversial nutrients that potentially affect preterm neurodevelopment: Essential fatty acids and iron. Paed Research. 2005; 57: 99 – 103.
15. Berglund S, Westrup B, Domellof M. Iron supplements reduce the risk of iron deficiency anemia in marginally low birth weight infants. Pediatrics. 2010, 126: 874-883.
16. Shao J, Rao R, Georgiff MK, Kaciroti N, Felt BT, Zhao Z, et al. Maternal serum ferritin concentration is positively associated with newborn iron stores in women with low ferritin status in late pregnancy. Nutr. 2012; 142: 2004-2009. Shao J, Lou J, Rao R, Georgieff MK, Kaciroti N, Felt BT, Zhao ZY, Lozoff B. Maternal serum ferritin concentration is positively associated with newborn iron stores in women with low ferritin status in late pregnancy. J Nutr. 2012 Nov;142(11):2004-9. doi: 10.3945/jn.112.162362. Epub 2012 Sep 26. PMID: 23014493; PMCID: PMC3498973.

https://pubmed.ncbi.nlm.nih.gov/23014493/ [References 9 and 16 have been repeated and the authors need to effect the changes so that what is now reference16 becomes reference 9 and reference 16 becomes reference 16 and the remaining numbers altered in the text and in the referencing section please]

17. Cusick SE, Georgieff MK, Rao R. Approaches for Reducing the Risk of Early-Life Iron Deficiency-Induced Brain Dysfunction in Children. Nutrients. 2018;10(2):227.
18. Rao R, Georgieff MK. Iron in fetal and neonatal nutrition. Semin Fetal Neonatal Med. 2007; 12: 54–63.
19. de Jong CL, Francis A, van Geijn HP, Gardosi J. Fetal growth rate and adverse perinatal events. Ultrasound Obstet Gynecol .1999; 13: 86–89.
20. Siddappa AM, Rao R, Long JD, Widness JA, Georgieff MK. The assessment of newborn iron stores at birth: A review of the literature and standards for ferritin concentrations. Neonatology. 2007; 92: 73–82.
21. Westby A, Miller L. Fetal Growth Restriction Before and After Birth. Am Fam Physician. 2021 Nov 1;104(5):486-492. PMID: 34783495.
22. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. Clin Med Insights Pediatr. 2016 Jul 14;10:67-83. doi: 10.4137/CMPed.S40070. PMID: 27441006; PMCID: PMC4946587.
23. Saloojee H, Pettifor JM. Iron deficiency and impaired child development. BMJ. 2001 Dec 15;323(7326):1377-8. doi: 10.1136/bmj.323.7326.1377. PMID: 11744547; PMCID: PMC1121846.
24. Rao R, Georgieff MK. Iron therapy for preterms. Clin Perinatol. 2009; 36: 27-42.
25. Jansson L, Holmberg L, Ekman R. Variation of serum ferritin in low birth weight infants with maternal ferritin, birth weight and gestational age. Acta Haematol 1979; 62: 273–277.
26. Haga P. Plasma ferritin concentrations in preterm infants in cord blood and during the early anemia of prematurity. Acta Pediatr Scand. 1980; 69: 637–641.
27. Siimes AS, Siimes MA. Changes in the concentration of ferritin in the serum during fetal life in singletons and twins. Early Hum Dev. 1986; 13: 47–52.
28. Carpani G, Marini F, Buscaglia M, Sinigaglia E, Moroni G. Red cell and plasma ferritin in normal fetuses at different ages of gestation. Eur J Haematol. 1992; 49: 260–262.
29. Bradley J, Leibold EA, Harris ZL, Wobken JD, Clarke S, Zumbrennen KB, et al. Influence of gestational age and fetal iron status on IRP activity and iron transporter protein expression in third-trimester human placenta. Am J Physiol Regul Integr Comp Physiol. 2004; 287: 894 - 901.
30. Mukhopadhyay K, Yadav RK, Kishore SS, Garewal G, Jain V, Narang A. Iron status at birth and at 4 weeks in preterm-SGA infants in comparison with preterm and term-AGA infants. J Matern Fetal Neonatal Med. 2012; 25: 1474-8.
31. Chen X, Scholl TO, Stein TP. Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: the Camden study Diabetes Care 2006; 29: 1077–1082.
32. Whitley E, Ball J. Statistics review 4: Sample size calculations. Critical Care .2002; 6: 335–341.
33. Lwanga SK, Tye C, Ayeni O. Teaching health statistics: Lesson and seminar outlines. 3rd ed. Geneva: WHO; 1999. p. 77.
34. World Health Organization/Centers for Disease Control and Prevention. Assessing the iron status of populations: a report of a joint World Health Organization/Centers for Disease Control technical consultation on the assessment of iron status at the population level. Geneva; 2004 April. Available at: http://whqlibdoc.who.int/publications/2004/9241593156_eng.pdf. Accessed January 4, 2008.

35. WHO. Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, 2011. Report No: WHO/NMH/NHD/MNM/11.2. Available at: http://www.who.int/vmnis/indicators/serum_ferritin.pdf. Accessed June 13, 2013.
36. Baker RD, Frank R. The Committee on Nutrition. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0 −3 years of age). Pediatrics 2010; 126: 1040 - 1050.
37. Griffin IJ, Reid MM, McCormick KP, Cooke RJ. Zinc protoporphyrin/haem ratio and plasma ferritin in preterm infants. Arch Dis Child Fetal Neonatal Ed/ 2002; 87: 49–51.
38. Pedro De Alard N, Werner E, Christensen RD, editors. Neonatal hematology: pathogenesis, diagnosis, and management of hematologic problems. Cambridge University Press; 2013. p. 40.
39. Conrad ME, Umbreit JN. Pathways of iron absorption. Blood Cell Mol Dis 2002; 29: 336-355.
40. Andrews NC, Schmidt PJ. Iron homeostasis. Annu Rev Physiol. 2007; 69: 69-85.
41. Sweet DG, Savage GA, Tubman R, Lappin TRJ, Halliday HL. Cord blood transferrin receptors to assess fetal iron status. Arch Dis Child Fetal Neonatal Ed. 2001; 85: 46–48.
42. Bazmamoun H, Narimani S, Shokouhi M, Esfahani H, Soltanian AR, Rastgoo Haghi AR. Evaluation of the Relationship Between Serum and Urine Ferritin Level of Low Birth Weight Infants. Iran J Pathol. 2022 Summer;17(3):323-327. doi: 10.30699/IJP.2022.546540.2807. Epub 2022 Aug 13. PMID: 36247497; PMCID: PMC9508545.
43. Agarwal R, Virmani D, Jaipal M, Gupta S, Sankar MJ, Bhatia S, Agarwal A, Devgan V, Gupta N, Deorari AK, Paul VK; Investigators of LBW Micronutrient Study Group. Iron stores in low and normal birth weight infants at birth and in early infancy. Indian J Pediatr. 2014 Mar;81(3):279-82. doi: 10.1007/s12098-013-1176-7. Epub 2013 Aug 27. PMID: 23979924.
44. Dallman PR. Iron deficiency anemia: a synthesis of current scientific knowledge and U.S. recommendation for prevention and treatment. In: Iron deficiency anemia, recommended guideline for the prevention, detection and management among U.S. children and women of child bearing age. Institute of Medicine, Washington, DC: National Academy Press, 1993:41–96
45. Faldella G, Alessandroni R, Salvioli GP, Capelli M, Paolini M, Minak G, Tirafeferri S. Lack of correlation between free erythrocyte porphyrin and serum ferritin values at birth and at 2 months of life in low birthweight infants. Arch of Dis Child. 1983 March 01; 58: 216-219.
46. Obladen M, Diepold K, Maier RF. Venous and arterial hematologic profiles of very low birth weight infants. Paediatrics. 2000; 106: 707-711.
47. Arad I, Konijn AM, Linder N, Goldstein M, Kaufmann NA. Serum ferritin levels in preterm infants after multiple blood transfusions. Am J Perinatol .1988; 5:40–43.
48. Olivares M, Llaguno S, Marin V, Hertrampf E, Milad M. Iron status in low birthweight infants, small and appropriate for gestational age. A follow up study. Acta Paediatr. 1992; 81: 824–828.