

Evaluation of the Relationship Between Serum and Urine Ferritin Level of Low Birth Weight Infants

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ABSTRACT

Background & Objective: Iron deficiency before birth or in infancy can cause long-term behavioral and neurological disorders. Measuring serum ferritin is an effective way to diagnose iron deficiency but requires significant blood volume from a low birth weight infant. Therefore, the present study was performed to investigate the relationship between serum and urinary ferritin levels in low birth weight infants.

Methods: In this cross-sectional study, 76 infants weighing less than 2500 g were studied. To measure serum ferritin level, 1.5 mL of blood and to measure urinary ferritin level, at least 1 mL of urine was collected from each infant. Then the results were compared. Data analysis was performed using SPSS software version 16, and the significance level was considered less than 0.05.

Results: Out of 76 neonates studied, 51.3% were boys, and 80.3% were premature infants. The mean birth weight of infants was 2056.31±318.74 g, and the mean serum and urinary ferritin levels were 134.77±72.35 and 85.55±70.97 ng, respectively. There was a statistically significant relationship between serum and urinary ferritin levels. Also, serum ferritin and urinary ferritin levels had a statistically significant relationship with birth weight and gestational age. The higher the birth weight as well as the age at birth, the higher the serum ferritin and urinary ferritin.

Conclusion: According to the findings of this study, measurement of urinary ferritin level can be used as a noninvasive tool for iron deficiency screening in low birth weight infants instead of serum ferritin level.

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Introduction

Iron is one of the most important micronutrients that play an important role in functioning of all vital systems of the body, especially the brain. When iron deficiency occurs in the prenatal or neonatal period, it can cause long-term behavioral and neurological disorders. (1, 2). Iron deficiency at birth is more common among high-risk groups, such as infants with low birth weight compared to gestational age, premature infants with very low birth weight, infants of diabetic mothers, and infants of mothers who smoke (3-6). Clinical signs of iron deficiency anemia include paleness, irritability, premature fatigue, muscle weakness, increased heart and respiration rate, enlarged heart and spleen, and decreased alertness, and can slow the child's normal growth and development. Therefore, timely diagnosis and treatment

of iron deficiency are very important, especially in infants and children (7-10).

Current iron deficiency screening methods focus more on the diagnosis of anemia. But anemia is a relatively late effect of iron deficiency and probably does not occur until the brain's iron deficiency causes a neurological defect in the infant. (7).

Ferritin is made from iron and a protein called Apo ferritin in the cell cytoplasm and is the best indicator for measuring iron stores in the body. According to studies, measuring serum ferritin is an effective method of identifying iron deficiency (11-14). However, the use of ferritin in low birth weight infants is limited due to the significant volume of blood required for phlebotomy, indicating the need for alternative screening in infants at

higher risk for iron deficiency. Elevated serum ferritin is seen in cases such as pregnant women with preterm labor and preterm PROM, as well as an acute phase reactant (15, 16)

Given the above, this study was performed to investigate whether measuring urinary ferritin levels can be used as a noninvasive tool for screening low-weight infants for iron deficiency.

Material and Methods

This cross-sectional study was performed in 2021 on 76 low birth weight infants (less than 2500 g) under 28 days who were born in Fatemeh Hospital in Hamadan. Neonates were randomly selected by the easy sampling method.

Inclusion criteria included age less than 28 days, weight less than 2500 grams at birth, and absence of infectious, inflammatory, liver, and kidney diseases in the infants.

Exclusion criteria included parental dissatisfaction and the impossibility of sampling the neonate for any reason.

After obtaining informed parental consent, 1.5 mL of blood from each infant was collected and centrifuged to measure serum ferritin. The supernatant was then transferred to the tube for testing within two hours. Serum ferritin level was measured by chemiluminescent immunoassay method (Mindray kit, China) and the results were reported in ng/mL. Within 24 hours after sampling, at least 1 mL of urine was collected using a urine bag to measure urinary ferritin. Urine ferritin was measured by a method similar to serum ferritin (CL-Mindray kit, China), and the results were reported in ng/mL.

Demographic data of patients were collected using a questionnaire.

Using statistical indices of mean and standard deviation, quantitative variables such as age, serum, and urine ferritin level were described. Contingency tables and percentages were used to describe qualitative data. Pearson's correlation coefficient was used to determine the relationship between serum and urine ferritin levels. Data analysis was performed using SPSS version 16 (SPSS Inc., Chicago, IL., USA), and the significance level was considered less than 0.05.

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Results

Of the 76 neonates, 39 (51.3%) were male, and 61 (80.3%) were preterm. The mean birth weight of infants was 2056.31 ± 318.74 g, and the mean serum and urine ferritin levels were 134.77 ± 72.35 and 86.55 ± 70.97 ng, respectively.

There was a statistically significant relationship between serum and urine ferritin levels. There was also a statistically significant relationship between serum and urine ferritin levels with birth weight and gestational age. There was a statistically significant relationship between birth weight and gestational age ([Table 1](#)).

Serum and urine ferritin levels were higher in male infants than in female infants, but this difference was not statistically significant ([Table 2](#)).

Serum and urine ferritin levels in term neonates were higher than in preterm neonates, which was statistically significant. ([Table 3](#)).

Table 1. Comparison of serum and urine ferritin levels with gestational age in low birth weight infants.

	Variable	Serum ferritin	Urine ferritin	Birth weight	Gestational age
Serum ferritin	Pearson's correlation coefficient	<i>r</i>	0.902**	0.119	0.363**
	P-value		0.000	0.3	0.001
Urine ferritin	Pearson's correlation coefficient		1	0.052	0.331**
	P-value			0.65	0.004
Birth weight	Pearson's correlation coefficient			1	0.353**
	P-value				0.002
Gestational age	Pearson's correlation coefficient				1
	P-value				

Table 2. Serum and urine ferritin levels in low birth weight infants.

Variable		Number	Mean± STD	P-value
Serum ferritin	Boy	39	141.58 ± 70.18	0.4
	Girl	37	127.58 ± 74.84	
Urinary ferritin	Boy	39	97.21 ± 75.37	0.18
	Girl	37	75.32 ± 45.15	

Table 3. Serum and urine ferritin levels in term and preterm low birth weight infants.

Variable		Number	Mean± STD	P-value
Serum ferritin	Term	15	148.88 ± 71.1	0.000
	Preterm	61	77.39 ± 44.48	
Urine ferritin	Term	15	98.25 ± 71.86	0.000
	Preterm	61	38.99±42.78	

Discussion

The results of this study showed that there is a statistically significant relationship between serum and urine ferritin levels. There was also a statistically significant relationship between serum and urine ferritin levels with birth weight and gestational age.

Unfortunately, in the literature review, few similar studies were found in this area for comparison.

In a pilot study by Baher *et al.* (2019), serum and urine ferritin levels in a limited number of healthy adult men (n=5), healthy term infants (n=5), and premature infants (n=8) as well as children with high ferritin levels due to iron overload or liver disorders (n=6), was measured. The results showed that serum and urinary ferritin levels were significantly correlated, similar to our study's results. The researchers suggested that measuring urinary ferritin levels could be used as an alternative screening method to diagnose iron deficiency in cases where blood sampling is limited (17).

In a study by Gerday E *et al.* (2021), performed at the PICU on 49 infants at risk for iron deficiency, there was a statistically significant relationship between urine and serum ferritin levels which was in line with the results of our study (18). One of the shortcomings of this study, as noted by the article's authors, is that the study focused on a selected subset of NICU patients at risk for iron deficiency, while in our study, there was no such limitation.

In another study by Ishikawa *et al.* (1982), conducted on healthy adults in Japan, there was a statistically significant relationship between serum and urine ferritin levels. Also, serum ferritin in healthy men (4.1 ng/mL) was significantly higher than in healthy women (1.8 ng/mL). This difference was also present in their urine ferritin levels (19). In our study, serum and urine ferritin levels were higher in male infants than in female infants, but this difference was not statistically significant.

In the study of Lipschitz *et al.* (1980), urine ferritin was measured by the immune-radiometric method in

healthy volunteers and patients with various hematological diseases. The average concentration of urine ferritin in normal individuals was 2.2 micrograms per liter, which was about 3% of serum ferritin level. An increase in urine ferritin level of up to 45 µg/L was observed in patients with malignancy, which was accompanied by a proportional increase in serum ferritin so that the urine ferritin level was still, on average 7% of serum ferritin. The highest levels of urine ferritin (mean 170 µg/L) were seen in chronic hemolytic anemia. In these patients, urine ferritin was disproportionately higher than serum ferritin (mean≈82%). Therefore, the result was that, in normal people and in malignant patients, the origin of urine ferritin is different because there is a link between urine ferritin and reticuloendothelial iron storage. In this case, the most likely source of urine ferritin is iron in renal tubular cells, which is in balance with the body's iron stores (20).

Conclusion

urine ferritin measurement can be used as a noninvasive tool to screen iron deficiency in low birth weight infants instead of serum ferritin.

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Conflict of Interest

The authors declared no conflict of interests.

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References

1. 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. [DOI:10.3390/nu10020227] [PMID] [PMCID]
2. Georgieff MK. The role of iron in neurodevelopment: fetal iron deficiency and the developing hippocampus. *Biochem Soc Trans*. 2008;36(Pt 6):1267-71. [DOI:10.1042/BST0361267] [PMID] [PMCID]
3. Kasper DC, Widness JA, Haiden N, Berger A, Hayde M, Pollak A, *et al*. Characterization and differentiation of iron status in anemic very low birth weight infants using a diagnostic nomogram. *Neonatology*. 2009;95(2):164-71. [DOI:10.1159/000153101] [PMID] [PMCID]
4. Lundström U, Siimes MA, Dallman PR. At what age does iron supplementation become necessary in low-birth-weight infants? *J Pediatr*. 1977;91(6):878-83. [DOI:10.1016/S0022-3476(77)80881-0]
5. MacQueen B, Christensen R, Ward D, Bennett S, O'Brien E, Sheffield M, *et al*. The iron status at birth of neonates with risk factors for developing iron deficiency: a pilot study. *J Perinatol*. 2017;37(4):436-40. [DOI:10.1038/jp.2016.234] [PMID] [PMCID]
6. Rasmussen KM. Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *J Nutr*. 2001;131(2):590S-603S. [DOI:10.1093/jn/131.2.590S] [PMID]
7. 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] [PMID] [PMCID]
8. Moradveisi B, Yazdanifard P, Naleini N, Sohrabi M. Comparison of Iron alone and Zinc Plus Iron Supplementation Effect on the Clinical and Laboratory Features of Children with Iron Deficiency Anemia. *Int J Hematol Oncol Stem Cell Res*. 2019;13(4):220-8. [PMID] [PMCID] [DOI:10.18502/ijhoscr.v13i4.1899]
9. Vieira ACF, Diniz AS, Cabral PC, Oliveira RS, Lóla MM, Silva SM, *et al*. Nutritional assessment of iron status and anemia in children under 5 years old at public daycare centers. *J Pediatr*. 2007;83:370-6. [DOI:10.2223/JPED.1680] [PMID]
10. Motlagh ME, Mardani M. Anemia and Iron deficiency anemia in Lorestan province. *Feyz J Kashan Univ Med Sci*. 1999;3.
11. Baker RD, Greer FR, Nutrition Co. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics*. 2010;126(5):1040-50. [DOI:10.1542/peds.2010-2576] [PMID]
12. Goodnough LT, Skikne B, Brugnara C. Erythropoietin, iron, and erythropoiesis. *Blood*. 2000;96(3):823-33. [DOI:10.1182/blood.V96.3.823] [PMID]
13. Mei Z, Cogswell ME, Parvanta I, Lynch S, Beard JL, Stoltzfus RJ, *et al*. Hemoglobin and ferritin are currently the most efficient indicators of population response to iron interventions: an analysis of nine randomized controlled trials. *J Nutr*. 2005;135(8):1974-80. [DOI:10.1093/jn/135.8.1974] [PMID]
14. Cook JD, Lipschitz DA, Miles LE, Finch CA. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr*. 1974;27(7):681-7. [DOI:10.1093/ajcn/27.7.681] [PMID]
15. Allen LH. Anemia and iron deficiency: effects on pregnancy outcome. *Am J Clin Nutr*. 2000;71(5 Suppl):1280S-4S. [DOI:10.1093/ajcn/71.5.1280s] [PMID]
16. Saha C, Jain V, Gupta I, Varma N. Serum ferritin level as a marker of preterm labor. *Int J Gynecol Obstet*. 2000;71(2):107-11. [DOI:10.1016/S0020-7292(00)00260-5]
17. Bahr TM, Christensen RD, Ward DM, Meng F, Jackson LK, Doyle K, *et al*. ferritin in serum and urine: A pilot study. *Blood Cells Mol Dis*. 2019;76:59-62. [PMID] [PMCID] [DOI:10.1016/j.bcmd.2019.02.001]
18. Gerday E, Brereton JB, Bahr TM, Elmont JO, Fullmer S, Middleton BA, *et al*. Urinary ferritin; a potential noninvasive way to screen NICU patients for iron deficiency. *J Perinatol*. 2021;41(6):1419-25. [DOI:10.1038/s41372-020-0746-6] [PMID]
19. Ishikawa K, Narita O, Saito H, Kato K. Determination of ferritin in urine and in serum of normal adults with a sensitive enzyme immunoassay. *Clin Chim Acta*. 1982;123(1-2):73-81. [DOI:10.1016/0009-8981(82)90115-2]
20. Lipschitz DA, Allegre A, Cook JD. The clinical significance of ferritinuria. *Blood*. 1980;55(2):260-4. [DOI:10.1182/blood.V55.2.260.260] [PMID]

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