

Original Research Article

Screening for iron deficiency in early childhood using serum ferritin

Abstract

Introduction: The iron deficiency is an important public health problem widely prevalent in the early childhood period. Iron is very important for various body processes like monoamine metabolism, synthesis of myelin, and metabolic function of the brain. It has many detrimental effects on the cognition, emotional, social, and motor development. Serum ferritin is an easily available, non invasive, inexpensive with high specificity for iron deficiency.

Aim: The present study was conducted with the aim to estimate the levels of hemoglobin and serum ferritin in young children in the age group of 1-5 years irrespective of their sex.

Materials and methods: Laboratory data of serum ferritin and hemoglobin levels were prospectively collected of apparently healthy children, 1 to 5 years of age coming to Pediatrics OPD of Acharya Shri Chander College of Medical Sciences, Jammu. The ferritin levels were estimated in roche chemiluminescent immunoassay. The haemoglobin levels were estimated. Children with serum ferritin level < 12 µg/L was considered as deficiency. The statistical analysis was conducted using SPSS version 20.

Results: A total of 100 children, 1 to 5 years of age were enrolled in the study. The mean hemoglobin level in children is 12.2gm%. The mean serum ferritin level in children is 29.2µg/L. In our study, it was observed that the mean Hb levels are higher in the reference age group, than decreases in the 2-3 year age group and then again increases in the 3-5 years age group. It was further observed that the serum ferritin levels were higher in the reference age group and then decreases in the 2-3 year age group. The serum ferritin levels further rises in the 3-4 years, 4-5 years age group.

Conclusion: In our study, it was observed that serum ferritin is a more reliable test than hemoglobin for screening iron deficiency in early childhood. The most favorable age group for screening for iron deficiency appears to be 2 to 3 years of age in which maximum number of children with iron deficiency was observed, but other associated conditions should also be kept in mind.

Keywords: serum ferritin, childhood, hemoglobin, iron deficiency.

Introduction

The deficiency of iron is one of the most common nutritional disorders that occur worldwide. Both in developing and developed countries, it is one of the major public health concerns.¹ It has been observed that the prevalence of iron deficiency is more during the early childhood, which is a crucial time for the developing brain development.²

The deficiency of iron has a negative brunt on neurodevelopmental outcomes.³ Iron is very important for the different processes occurring in the body like monoamine metabolism, synthesis of myelin, and metabolic function of the brain.² It has been observed in various animal studies that the deficiency of iron during the early post natal period alters development of brain and cognition.⁴ In the various human studies, it was observed that poor outcomes across multiple domains of child development are associated with the deficiency of iron.⁵ Those children who had iron deficiency in early childhood period, may present with impairments in cognitive, social, and emotional functioning during adolescence and young adulthood.⁶ The American Academy of Pediatrics (AAP) recommends universal screening for anemia in children at the age of 12 months through measurement of hemoglobin.⁷

Serum ferritin concentration is the most commonly deployed strategy used in clinical and public health settings, though many indexes are available.⁸ Ferritin is an iron storage protein; its post transcriptional regulation is done by iron-responsive elements in its messenger RNA and depends on the cellular iron status. The expression of ferritin depends on the iron concentration in the cell, higher iron concentration results in increased ferritin expression, whereas deficiency of iron inhibits its expression.⁹ The ferritin that we measure in the serum is mainly derived from macrophages,¹⁰ and does not contain storage iron but it only reflects overall storage form of iron and concentration of ferritin in the liver and other tissues.¹¹

In India, in primary health care centers, no recommendation is there for screening young children for iron deficiency or anemia. Therefore, keeping these things in mind, the present study was conducted with the aim to estimate the levels of hemoglobin and serum ferritin in young children in the age group of 1-5 years irrespective of their sex.

Material and methods

The present cross sectional study was conducted in the Department of Pediatrics, Acharya Shri Chander College of Medical Sciences, Jammu, in which the serum ferritin and hemoglobin was estimated in 100 apparently healthy children, 1-5 years of age coming to Pediatrics OPD. The sampling technique used is random sample collection. The apparently healthy children in the age group of 1-5 years are included in the study. Children with mild, severe or life threatening systemic diseases were not included in the study. Other exclusion criteria included children with a history of chronic illnesses, autoimmune diseases or recurrent fractures, children undergoing diagnostic biopsies, bronchoscopy or endoscopy and children on medication known to affect serum iron or ferritin levels, children on iron supplementation. The study was approved by the institutional ethics committee. Personal and demographic data of children were collected. Blood samples

were collected in plain vacutainers and EDTA vacutainers. The ferritin levels were estimated in abbot architect chemiluminescent microparticle immunoassay.¹² The haemoglobin levels were estimated.

In the present study, children with serum ferritin level $< 12 \mu\text{g/L}$ was considered as deficiency. The statistical analysis was conducted using SPSS version 20. Descriptive statistics were used to present the clinical characteristics of the participants. Continuous variables were described using the means and standard deviation. All 'p' values were two sided and $p > 0.05$ was considered to be statistically significant.

Results

A total of 100 children, 1 to 5 years of age were enrolled in the study. The mean hemoglobin level in children is 12.2gm%. We compared the mean hemoglobin levels in different age groups taking the 1 -2 years age group as reference group. It was observed that the mean hemoglobin level in the reference age group i.e. 1-2 years is 11.9 gm%. Whereas in the 2-3 years age group, the mean Hb level was less than the reference group and the difference was statistically significant. The higher Hb levels were observed in the 3-4 years but not statistically significant. In the 4-5 years age group, the mean Hb levels are higher than the reference group and the difference was statistically significant. The 2-3 year age group had higher percentage of children with deficient Hb levels.

The mean serum ferritin level in children is $29.2 \mu\text{g/L}$. We compared the mean serum ferritin levels in different age groups taking the 1 -2 years age group as reference group. It was observed that the mean serum ferritin level in the reference age group i.e. 1-2 years is $36.8 \mu\text{g/L}$, whereas, in the 2-3 years age group, the mean serum ferritin Hb level was less as compared to the reference group and the difference was statistically significant. The higher serum ferritin levels were observed in the 3-4 years and 4-5 years age group than the reference group and the difference was statistically significant. The 2-3 year age group had higher percentage of children with deficient serum ferritin levels.

Discussion

In our study, it was observed that the mean Hb levels are higher in the reference age group, than decreases in the 2-3 year age group and then again increases in the 3-5 years age group. It was further observed that the serum ferritin levels were higher in the reference age group and then decreases in the 2-3 year age group. The serum ferritin levels further rises in the 3-4 years, 4-5 years age group. The deficiency of iron is an important public health problem and with higher prevalence in the early childhood period. Iron deficiency has many detrimental effects on the cognition, emotional, social, and motor development.¹³ The deficiency of iron due to non-anemic reasons usually identified at the latent stage, and should be identified before its progression to iron deficiency anemia. Serum ferritin is an easily available, non invasive, inexpensive with high specificity for iron deficiency.¹⁴ Our results are similar with a study done by Oatley, in which screening strategy for iron deficiency in young children was evaluated, and it was found that serum ferritin levels decreases at the age from 12 to 15 months whereas in the children above 2 years of age, serum ferritin level

increases. The rate of change in Hb levels upto 2 years of age were not significant, while in children above 2 years of age, with increase in age, there was increase in Hb levels. At 12 months of age, Hemoglobin may be more reflective of an infant's budding capacity for iron homeostasis, rather than any pathological state, which may further improve with increase in age. The detection of anemia only by measurement of hemoglobin, lacks specificity to detect iron deficiency, as there are other causes of decrease in hemoglobin like hemoglobinopathies and other nutritional deficiencies. Though acute inflammation is one of the cause of raised ferritin levels but it is uncommon among healthy young children attending health care centre for routine check ups.¹⁵

As per the recommendation of The American Academy of Pediatrics (AAP), universal screening of children for anemia by measuring Hb levels should be done at 12 months of age. As AAP, when the Hb levels <110g/L, it is defined as Anemia, or when serum ferritin level is <12µg/L, it is known as Iron deficiency.¹⁶

In our study, out of total 100 children, 14% had Hb levels below normal whereas 13% had serum ferritin below 12µg/l. For each of the 4 age categories, the mean ferritin (SD) as well as the proportion of children with ferritin <12µg/L are shown in Table 2 for the total sample and the mean hemoglobin (SD) as well as the proportion of children with hemoglobin <11gm% are shown in Table 1 for the total sample.

Out of 4 age categories, the age category between 2 to 3 years had the highest proportion of children with hemoglobin values <11gm% whereas the age category between 1 to 2 years had the highest proportion of children with hemoglobin values >11gm% (table 1). The highest proportion of children in the age group between 2 to 3 years were having low levels of serum ferritin below 12µg/L whereas highest proportion of children having high levels were seen in age group between 1 to 2 years (table 2).

Above obtained findings suggest that for diagnosing iron deficiency in children; hemoglobin is not an ideal investigation and its cutoff limit for anemia may require to be reconsidered. At 12 months of age, Hb may be more insightful of an infant's capacity to develop homeostasis of iron, rather than pathological conditions, which may get better with increase in age.¹⁶ Also, only measurement of Hb levels to determine anemia in iron deficient children lacks specificity, as there are many other causes of decreased hemoglobin levels such as hemoglobinopathies and nutritional disorders.⁷

Given our finding that iron deficiency peaks between 2 to 3 years, this would allow most cases to be identified. The World Health Organization recommends that serum ferritin should be used to measure the iron status in population surveys and for program evaluation.¹⁷ In the principles that was published by the World Health Organization in the year 1968, it was suggested that in primary care settings, serum ferritin was used for screening of iron deficiency.¹⁸ To effectively correct iron deficiency, various oral iron supplements are available in the market.¹⁹ The professional organizations such as AAP finally recommended the policy to screen for iron deficiency.⁷

Conclusions

It was concluded from our study that serum ferritin is a more reliable test than hemoglobin for screening iron deficiency in early childhood. The most favorable age for screening for iron deficiency using serum ferritin

appears to be 2 to 3 years of age in which maximum number of children with iron deficiency was observed. While evaluating a child for iron deficiency, the other acute inflammatory conditions which affect the serum ferritin levels should also be taken into consideration. Hence, a screening strategy is needed for evaluation of a child presenting with iron deficiency.

References

1. World Health Organization. The Global Prevalence of Anemia in 2011. Geneva, Switzerland: World Health Organization; 2015. Available at: www.who.int/nutrition/publications/micronutrients/global_prevalence_anaemia_2011/en/. Accessed August 2, 2021.
2. Georgieff MK. Iron assessment to protect the developing brain. *Am J Clin Nutr.* 2017;106 (suppl 6):1588S–1593S.
3. Lozoff B, Clark KM, Jing Y, Armony-Sivan R, Angelilli ML, Jacobson SW. Dose-response relationships between iron deficiency with or without anemia and infant social-emotional behavior. *J Pediatr.* 2008;152(5):696–702.
4. Georgieff MK, Brunette KE, Tran PV. Early life nutrition and neural plasticity. *Dev Psychopathol.* 2015;27(2):411–423.
5. Leyshon BJ, Radlowski EC, Mudd AT, Steelman AJ, Johnson RW. Postnatal iron deficiency alters brain development in piglets. *J Nutr.* 2016;146(7):1420–1427.
6. Carter RC, Jacobson JL, Burden MJ, Sivan RA, Dodge NC, Angelilli ML, et al. Iron deficiency anemia and cognitive function in infancy. *Pediatrics.* 2010;126(2):e427-e434.
7. Baker RD, Greer FR. Committee on Nutrition American Academy of Pediatrics. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics.* 2010;126(5):1040–1050.
8. Mei Z, Cogswell ME, Parvanta I, Lynch S, Beard JL, Stoltzfus RJ. 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;135:1974–80.
9. Muckenthaler MU, Galy B, Hentze MW. Systemic iron homeostasis and the iron-responsive element/iron-regulatory protein (IRE/IRP) regulatory network. *Annu Rev Nutr.* 2008;28:197–213.

10. Cohen LA, Gutierrez L, Weiss A, Leichtmann-Bardoogo Y, Zhang DL, Crooks DR, et al. Serum ferritin is derived primarily from macrophages through a non-classical secretory pathway. *Blood*. 2010;116:1574–84.
11. Garcia Casal MN, Pasricha SR, Martinez RX, Lopez-Perez L, Pena Rosas JP. Serum or plasma ferritin concentration as an index of iron deficiency and overload. *Cochrane Database Syst Rev*. 2015;7:CD011817. Corpus ID:73228711.
12. National committee for clinical laboratory standards. Evaluation of precision performance of clinical chemistry devices; tentative guideline-second edition. NCCLS. Document EP5-T2. Villanova, PA: NCCLS;1992.
13. Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status: a longitudinal analysis of cognitive test scores to age 19 years. *Arch Pediatr Adolesc Med*. 2006;160(11):110–11.
14. Pfeiffer CM, Looker AC. Laboratory methodologies for indicators of iron status: strengths, limitations, and analytical challenges. *Am J Clin Nutr*. 2017;106(suppl 6):1606S–1614S.
15. Oatley H, Borkhoff CM, Chen S, Macarthur C, Persaud N, Birken CS, et al. Screening for Iron Deficiency in Early Childhood Using Serum Ferritin in the Primary Care Setting. *Pediatrics*. 2018;142(6):e20182095. PMID: 30487142.
16. Lonnerdal B. Development of iron homeostasis in infants and young children. *Am J Clin Nutr*. 2017;106(suppl 6):1575S–1580S.
17. Lynch S. The rationale for selecting and standardizing iron status indicators. In: World Health Organization, ed. *World Health Organization Report: Priorities in the Assessment of Vitamin A and Iron Status in Populations*. Report, 15–17 September, 2010, Panama City, Panama. Geneva, Switzerland: World Health Organization; 2012:55–62.
18. Wilson JMG, Jungner G. *Principles and Practice of Screening for Disease*. Geneva, Switzerland: World Health Organization; 1968.
19. Powers JM, Buchanan GR, Adix L, Zhang S, Gao A, McCavit TL. Effect of low-dose ferrous sulfate vs iron polysaccharide complex on hemoglobin concentration in young children with nutritional iron-deficiency anemia: a randomized clinical trial. *JAMA*. 2017;317(22):2297–2304.

Table 1: Haemoglobin levels in different age groups and proportion of children with haemoglobin levels less than 11 gm%

Age (in years)	N	Mean±SD	Percentage below 11gm%	p value
Total Samples	100	12.2±1.1	14	
1-2 years	31	11.9±1.8	9.6	
2-3	24	10.8±1.1	12.5	0.01*
3-4	19	12.3±1.5	10.5	0.4
4-5	26	12.8±1.3	11.5	0.03*
*p-value <0.05, is considered significant				

Table 2: Serum ferritin levels in different age groups and proportion of children with ferritin levels less than 12 µg/L

Age (In years)	N	Mean±SD	Percentage below 12 µg/L	p value
Total Samples	100	29.2±11.4	13	
1-2 year	31	36.8±14.6	6.4	
2-3	24	24.8± 6.2	16.6	0.001*
3-4	19	27.3±8.1	15.7	0.006*
4-5	26	28.4±9.7	7.6	0.01*
*p-value <0.05, is considered significant				