Ultrasonography and Doppler ultrasonography findings of children with iron deficiency anemia

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Abstract

Aim: Iron deficiency anemia (IDA) is an important health problem in children in the worldwide. It affects both growth and mental motor development. Iron decrease then irons deficiency (ID) occurs during the developing of IDA. In the literature, there is no information about ultrasonography (US) and Doppler US findings in the development of IDA. The aim of this study is to search the US and Doppler US findings of liver, spleen and main vascular structures of children with the iron decrease, ID, and IDA.
Material and Methods: This study including 160 patients who have the iron decrease (n=43), ID (n=52), and IDA (n=65) in laboratory findings. The control group was 50 children. The liver and spleen sizes with parenchymal echogenicity, CCA Vmax -Vmin, ICA Vmax -Vmin, their pulsatility (PI) and resistive index (RI) were measured.
Results: 23 patients (35%) were diagnosed with hepatomegaly and 8 patients (12%) were diagnosed with splenomegaly having IDA. There was a statistically significant difference between the groups in terms of CCA Vmax -Vmin, ICA Vmax -Vmin, and also RI - PI index of CCA with ICA ($p < 0.05$).
Conclusion: Hepatomegaly and splenomegaly can be seen in IDA. Increasing of anemia cause changes in the vascular flow velocities, and also increase the blood volume of the brain. If anemia is detected at an early stage and treatment is regulated, cognitive disturbances will not occur in children. In the diagnosis, an US and a Doppler US examination are useful.

Keywords: Iron Decrease; Iron Deficiency; Iron Deficiency Anemia; Doppler Ultrasonography.

INTRODUCTION

According to the World Health Organization (WHO), anemia is defined in a man below 14 g/dl, in a woman below 12 g/dl of hemoglobin. Anemia due to iron (Fe) deficiency is called iron deficiency anemia (IDA) and takes the first place among the causes of anemia (1). IDA is the most common form of anemia in societies with low socioeconomic status as well as in developed societies. In developed countries, prevalence is 4-20%, while in underdeveloped countries it is 80% in children (2-4). In our country, it was around 10-85% ratio in different studies (5,6).

During the childhood and especially during the infancy period, the iron requirement increases due to the fact that growth and development are fast. Again, the absence of adequate iron in the nutrients of this cycle, IDA is most common in this age group. IDA is an important health problem in this period because it affects both growth and mental motor development (7,8).

A number of biochemical and hematological changes occur in the progressive iron deficiency. First, there is a loss of hemosiderin from the iron deposits in the tissues and bone marrow. Iron decrease and iron deficiency (ID) occur before the development of IDA.

In the literature, radiological findings that could occur in iron deficiency, ID and IDA were not investigated. The purpose of this study is to investigate ultrasonography (US) and Doppler US findings of liver, spleen and main vascular structures in children with the iron decrease, ID, and IDA.

MATERIAL and METHODS

An approval of the study from the institutional Ethics Committee is approved. The study was conducted in accordance with the principles of the Declaration of Helsinki. A control group consisting of 160 patients who were diagnosed as iron decrease (n = 43), ID (n = 52) and IDA (n = 65) according to laboratory values. Control healthy group was 50 children. In radiology clinic, the US findings of liver, spleen, and Doppler US findings of left CCA, ICA are investigated. Power Doppler was used for investigating. Multi-frequency convex and linear transducer probes were used. No preparations were made for the children.

Hemoglobin values; It is considered to be 10.5 g/dl between 4 months and 2 years, 11.5 g/dl between 2 and 6 years, 12 g/dl between 6-12 years and less than 12 g/dl between 12-18 years It was. It is accepted as iron decrease if hemoglobin, serum iron, and transferrin saturation are normal and ferritin value is below12 ng /ml. It is accepted as ID if Hemoglobin is normal, serum iron is decreased, and 16% below transferrin saturation and ferritin below 12 ng /ml. IDA was considered to be a decreased hemoglobin level, decreased serum iron, less than 16% of transferrin saturation, and a ferritin level of less than 12 ng/ml (44).

The liver size was measured vertically on the midclavicular, where the right kidney was seen most widely. Spleen size was measured vertically from where it was seen most. The liver and spleen parenchyma characteristics were evaluated, comparing the parenchymal echogenicity with the renal parenchymal echogenicity.

The left CCA and CCA evaluation; Spectral measurements were taken with Doppler US. When the current spectrum was evaluated, the separation of the ICA and ECA was made by localization and the presence of ICA in the low resistance. In the longitudinal plane, the sampling range was placed in the middle of the lumen and in parallel. Current spectra were obtained with a Doppler angle of 45-60 degrees. Flow samples were taken from the CCA at least 1 cm proximal to the bifurcation and in the ICA scan, from the segment where the highest velocity values were measured. Left CCA and ICA Vmax, Vmin, RI and PI measurements were performed in the study. Measurements were obtained by the instrument's automatic measurement technique over the most clearly observed wave of the current pattern.

Statistical Analysis

The liver and spleen sizes were compared with normal values according to the age groups in the literature. The Independent-Samples T test was used for statistical evaluation of vascular parameters. Values of $p < 0.05$ were considered significant in the study.

RESULTS

In the study group, 69 (43%) were girls, 91 (57%) were boys. In the control group, 21 (42%) were girls and 29 (58%) were boys. Their ages ranged from 1 to 15 years (average 3-7 years). There was no significant difference between groups in terms of age and gender (p> 0.05).

In the IDA group, 23 cases (35%) had hepatomegaly (HM) and 8 cases (12%) had splenomegaly (SM). No significant pathological changes were observed in the liver and spleen parenchymal echogenicity. In comparison with the control group, there was no significant difference between left CCA Vmax, Vmin, ICA Vmax, Vmin, RI and PI values in the iron decrease group (p> 0.05) (Table 1).

In the ID group; CCA Vmax - Vmin and ICA Vmax - Vmin values were statistically significant (p <0.05) (Table 2). In the comparison of the IDA with the control group; there was a statistically significant difference between the values of CCA Vmax - Vmin, ICA Vmax - Vmin, CCA RI - PI and ICA RI - PI values (p <0.05) (Table 3).

In the comparison of the iron decrease and ID group; There was no significant difference between the groups (p> 0.05)

(Table 4). There was a statistically significant difference between CCA Vmax- Vmin, CCA RI, and ICA Vmax- Vmin values in the comparison of the iron decrease and IDA groups (p <0.05) (Table 5). There was no statistically significant difference between groups in the ID and IDA (p> 0.05) (Table 6).

Table 1. Comparison of CCA and ICA with iron decrease group and control group

	Iron decrease group (n:43)	Control group (n:50)	P Value
CCA Vmax	126,01±18,53	123,45±22,28	P=0,713
CCA Vmin	33,52±10,28	31,52±9,48	P=0,693
CCA RI	0,68±0,03	0,68±0,07	P=0,147
CCA PI	1,46±0,16	1,47±0,18	P=0,267
ICA Vmax	125,19±13,42	121,68±21,12	P=0,142
ICA Vmin	38,47±6,67	36,33±12,14	P=0,372
ICA RI	0,64±0,06	0,65±0,08	P=0,367
ICA PI	1,35±0,34	1,37±0,19	P=0,873

Table 2. Comparison of CCA and ICA with ID group and control group

	ID group (n:52)	Control group (n:50)	P Value
CCA Vmax	132,37±10,43	123,45±22,28	P=0,005
CCA Vmin	38,13±8,4	31,52±9,48	P=0,001
CCA RI	0,65±0,07	0,68±0,07	P=0,843
CCA PI	1,43±0,18	1,47±0,18	P=0,218
ICA Vmax	127,37±11,31	121,68±21,12	P=0,003
ICA Vmin	43,18±14,48	36,33±12,14	P=0,002
ICA RI	0,63±0,01	0,65±0,08	P=0,422
ICA PI	1,33±0,13	1,37±0,19	P=0,324

Table 3. Comparison of CCA and ICA with IDA group and control group

	IDA group (n:65)	Control group (n:50)	P Value
CCA Vmax	138,33±15,32	123,45±22,28	P=0,004
CCA Vmin	40,13±9,48	31,52±9,48	P=0,003
CCA RI	0,61±0,02	0,68±0,07	P=0,001
CCA PI	1,40±0,21	1,47±0,18	P=0,005
ICA Vmax	141,43±21,13	121,68±21,12	P=0,001
ICA Vmin	48,36±11,12	36,33±12,14	P=0,002
ICA RI	0,60±0,02	0,65±0,08	P=0,001
ICA PI	1,30±0,11	1,37±0,19	P=0,005

Table 4. Comparison of CCA and ICA with iron decrease group and ID group

	Iron decrease group (n:43)	ID group (n:52)	P Value
CCA Vmax	126,01±18,53	132,37±10,43	P=0,615
CCA Vmin	33,52±10,28	38,13±8,43	P=0,542
CCA RI	0,68±0,03	0,65±0,07	P=0,233
CCA PI	1,46±0,16	1,43±0,18	P=0,321
ICA Vmax	125,19±13,42	127,37±11,31	P=0,182
ICA Vmin	38,47±6,67	43,18±14,48	P=0,211
ICA RI	0,64±0,06	0,63±0,01	P=0,422
ICA PI	1,35±0,34	1,33±0,13	P=0,621

Table 5. Comparison of CCA and ICA with iron decrease group and IDA group

	Iron ecrease group (n:43)	IDA group (n:65)	P Value
CCA Vmax	126,01±18,53	138,33±15,32	P=0,002
CCA Vmin	33,52±10,28	40,13±9,48	P=0.003
CCA RI	0,68±0,03	0,61±0,02	P=0,001
CCA PI	1,46±0,16	1,40±0,21	P=0,467
ICA Vmax	125,19±13,42	141,43±21,13	P=0,001
ICA Vmin	38,47±6,67	48,36±11,12	P=0,001
ICA RI	0,64±0,06	0,60±0,02	P=0,632
ICA PI	1,35±0,34	1,30±0,11	P=0,378

Table 6. Comparison of CCA and ICA with ID group and IDA group

	Iron ecrease group (n:43)	IDA group (n:65)	P Value
CCA Vmax	132,37±10,43	138,33±15,32	P=0,288
CCA Vmin	38,13±8,43	40,13±9,48	P=0,324
CCA RI	0,65±0,07	0,61±0,02	P=0,652
CCA PI	1,43±0,18	1,40±0,21	P=0,327
ICA Vmax	127,37±11,31	141,43±21,13	P=0,621
ICA Vmin	43,18±14,48	48,36±11,12	P=0,366
ICA RI	0,63±0,01	0,60±0,02	P=0,517
ICA PI	1,33±0,13	1,30±0,11	P=0,197

DISCUSSION

Iron is an essential element for body functions. The development of mental-motor behaviors, learning events, social activities, functions related to cognition and understanding, immune system maturation, hormonal metabolism, and reproductive system are related to iron element (4,7,8). The high prevalence of IDA in various studies indicates an important social problem. The incidence of IDA is high in infants. School-age and preadolescent periods are less common in children (1,6).

Iron deficiency is not only a hematologic event that leads to anemia but a systemic disorder that affects many organs. Therefore, the effects of iron deficiency on the organism, the research of the prevention and treatment programs will continue intensively (9,10).

The iron balance in the body is provided by the close relationship between functional and storage iron. The iron is the functional compartment essentially in the hemoglobin. The storage of ferritin and hemosiderin is a smaller and more variable compartment. In case of a sudden usage of functional iron, the depot iron is used urgently. The depot iron is localized in the bone marrow reticuloendothelial system cells, liver and spleen.

The first and the basic method in the radiological examination of the liver and spleen is the US. In the US, normal liver parenchyma has homogeneous thin echo sample. The echogenicity is slightly higher than the spleen and kidney, lower than the pancreatic echogenicity. Obesity, alcoholism,nutrition, chemotherapy, steroids, diabetes, and Cushing disease cause a diffuse increase in echogenicity. Hepatitis and Budd-Chiari syndrome causes a diffuse decrease in echogenicity.

The shape and size of the spleen vary in different individuals, in different periods of life. In childhood age group, normal values according to age were reported in the US (11). A normal spleen presents a homogeneous, uniform, liver-like echo pattern in the echogenic capsule. Its echogenicity is slightly lower than the liver, slightly elevated from the adjacent renal parenchyma. Splenomegaly is associated with decreased echogenicity, lymphoma, and leukemic infiltration, and echogenicity increases hematologic diseases (12).

In our study, the increase in the size of the liver and spleen was assessed as an increased frequency of common infection with IDA. Lymphocyte and neutrophil dysfunction in iron deficiency is generally seen as causing infections. In children with iron deficiency, the percentage of T lymphocytes decreases. In addition, the killing capacity of bacteria such as E. coli, which results in neutrophil dysfunction is also reduced (13).

IDA is also known to have an effect on functions related to psychomotor development and comprehension. It is reported that cognitive functions are affected even in cases of mild anemia with an hemoglobin value less than 11 g/dl and iron deficiency that has not yet developed anemia (7,8,14). Studies have shown that endogenous opiates, known to have a negative effect on learning and memory, are increasing in the early period of ID and that myelination is also impaired in cases with ID (15).

The Doppler parameters of Vmax, Vmin, PI, RI, and Vmean can be used to assess vascular hemodynamics. In our study, we used Vmax, Vmin, RI, and PI in assessing changes in blood flow of the carotid arteries. High RI and PI values indicate increased resistance, while lower values indicate reduced resistance (12).

In our study; compared with the control group, reduced RI and PI values show that decreasing hemoglobin and deepening of the anemia increase the volume of blood reaching to the brain in order to increase the amount of hemoglobin.

Limitations of our study is that Doppler US measurements in child groups may be artifacts due to difficulties in positioning. The measurement errors may be results of motion. However, in the US evaluation of abdomen, it is difficult to evaluate due to intensive intestinal gas supposition in some patients because of the lack of fasting diet. There are some difficulties due to respiration and movement in infantile age groups.

CONCLUSION

To the best of our knowledge, this is the first study to reveal US and Doppler US findings of the iron decrease, ID, and IDA in the literature. Our present findings suggest that IDA changes in internal organs and vascular structures during the developmental process. Early diagnosis and treatment of the anemia, which is common in children, will prevent

the occurrence of permanent impairments. Diagnosis and follow-up of the cases may be useful for radiological examination of the US and Doppler US.

REFERENCES

1. Moy RJ. Prevalence, consequences and prevention of childhood nutritional iron deficiency: a child public health perspective. Clin Lab Hematol 2006;28(5):291-8.
2. Lin TF, Huang JN, Cash HL. Comprehensive review of preschool age anemia in the pacific island jurisdictions. Hawaii J Med Public Health 2017;76(1):331-6.
3. Lebso M, Anato A, Loha E. Prevalence of anemia and associated factors among pregnant women in Southern Ethiopia: A community based cross-sectional study. PLoS One 2017;12(12): e0188783.
4. McKee SG, Close R, Lowenthal E. Evaluation of Iron Deficiency Anemia in a Pediatric Clinic in the Dominican Republic. Ann Glob Health 2017;83(3-4):550-6.
5. Öznur Küçük, Ayşe Yeşim Göçmen, Suat Biçer. İştahsızlığı olan çocuklarda demir eksikliği anemisi sıklığı. Bozok Tıp Derg 2013; 2: 37-41.
6. Eroğlu Y, Hiçsönmez G. Hacettepe üniversitesi çocuk hastanesinde anemi sıklığı. Çocuk Sağ Hast Derg 1994;37:267-72.
7. Basu S, Kumar D, Anupurba S, Verma A, Kumar A. Effect of maternal iron deficiency anemia on fetal neural development. J Perinatol 2017;12.
8. Pala, E, Erguven, M, Guven, S, Erdogan, M, Balta, T. Psychomotor development in children with iron deficiency and iron-deficiency anemia. Food and Nutr Bull 2010;31(3): 431-5.
9. Girelli D, Ugolini S, Busti F, Marchi G, Castagna A. Modern iron replacement therapy: clinical and pathophysiological insights. Int J Hematol 2018;107(1):16-30.
10. Munoz M, Gomez-Ramirez S, Bhandari S. The safety of available treatment options for iron-deficiency anemia. Expert Opin Drug Saf 2018;17(2):149-59.
11. Rosenberg HK, Markowitz RI, Kolberg H, Park C, Hubbard A, Bellah RD. Normal splenic size in infants and children: sonographic measurements. AJR am J Roentgenol 1991; 157(1):119-21.
12. Tuncel E. Klinik radyoloji. 2. Baskı. Bursa: Güneş, Nobel, 2012.
13. Arica V, Arica S, Tutanç M, Edirne T, Gücük S, Motor S. 1-15 Yaş Arası Çocuklarda Demir Eksikliği Taramasında MCV ve RDW Ölçümü. F.Ü.Sağ Bil Tıp Derg 2011;25(1):1-4.
14. Deinard AS, List A, Lindgren B, Hunt JV. Chang PN. Cognitive deficits in iron deficient and iron-deficient anemic children. J Pediatr 1986;108(5 pt 1):681-9.
15. Kürekci AE, Sarici SU, Karaoglu A, Ulas HU, Atay AA, Serdar MA, et al. Effects of iron deficiency versus iron deficiency anemia on brainstem auditory evoked potentials in infancy. Turk J Pediatr 2006;48(4):334-9.