The Egyptian Journal of Hospital Medicine (January 2025) Vol. 98, Page 1342- 1349

Indicators of Response to Oral Iron Therapy in Children with Iron Deficiency Anemia; A Cross-Sectional Study

Mona Hassan[1], Sherine Shalaby[2], Eman Shaheen[3], Islam Hatem[1], Mohammad Mahmoud El- Naghi[1]
[1]Department of Pediatrics, Faculty of Medicine, Helwan University, Cairo, Egypt
[2]Department of Pediatrics, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[3]Department of Clinical and Chemical Pathology, Faculty of Medicine, Helwan University, Cairo, Egypt
***Corresponding author:** Mona Hassan, **E-mail:** Mona.hassan@med.helwan.edu.eg
Phone number: 002 01007584490, **ORCID number:** 0000-0003-2630-5358

ABSTRACT

Background: Iron deficiency anemia (IDA), is the most common micronutrient deficiency in the world especially in children. It is important to early manage IDA and follow up iron therapy response to minimize later on complications.
Purpose: The authors aimed to determine the demographic, clinical and laboratory indicators for the response to oral iron therapy in Egyptian children with iron deficiency anemia.
Patients and Methods: This cross-sectional study conducted at Helwan University Hospital at Badr city, Egypt on 48 Egyptian children with (IDA) aged 1-7 years. Children received oral iron in a daily dose of 6 mg/kg/day elemental iron for 3 months. Children who showed increased hemoglobin level at follow up were included. Complete blood count was included from the patient files and serum ferritin levels before and after iron therapy.
Results: Following oral iron therapy, the hemoglobin, mean platelet volume, and ferritin values showed a significant increase, while red cell distribution width showed a significant decrease. Children with range 2-4 weeks of therapy the response was < 1 gm and children with 2-5 weeks range of iron therapy the response was > 1 gm.
Conclusions: The study revealed that the longer duration of oral iron therapy was associated with good response. The hemoglobin, mean platelet volume and ferritin values showed a significant increase following oral iron therapy, while red cell distribution width values showed a significant decrease. In our results there was no laboratory parameter can predict the response to oral iron therapy.
Keyword: Iron deficiency anemia, Response to therapy, oral iron, Children

INTRODUCTION

Anemia is considered the most common hematological disorder in the world. Children under 5 years old and school children are considered one of the most affected groups with anemia. About 42% of those preschool children are anemic, developmental delay and behavioral problems are considered some of the anemic problems that appear in preschool children [(1)].

Iron deficiency anemia (IDA), is the most common single micronutrient deficiency in the world. Iron deficiency (ID) is responsible for Up to 50% from all types of anemia. Anemia caused by ID is the most prevalent type in developed and developing countries [(2)]. Iron plays essential role in many functions including growth and development. ID impairs motor, cognitive, and immune system development and leads to long term developmental delay if left untreated. The most common causes of ID in children include inadequate dietary intake together with rapid growth, blood loss and malabsorption disorders [(3)].

Oral iron therapy is the preferred treatment options because it is effective, inexpensive and has minimal side effects. The success of oral iron therapy is usually evaluated by monitoring multiple clinical and hematological parameters such as hemoglobin level, mean corpuscular volume (MCV), red cell distribution width (RDW), reticulocyte count, mean platelet volume (MPV) and serum ferritin. These parameters improve sequentially over time and their monitoring help to predict the response and improve the effectiveness of treatment [(4)].

Response to oral iron therapy varies depending on severity of anemia, adherence to treatment, and health status. Generally, showing improved hemoglobin (Hb) levels about 1 g/dl within two to four weeks of starting treatment is considered a good initial response [(5,6)]. Iron therapy can elevate MCV in those with IDA because iron plays a crucial role in hemoglobin production, influencing the size and volume of red blood cells. As iron levels rise due to therapy, red blood cells expand in size, resulting in an MCV increase, it may take few months to return to normal [(7)]. Red blood cell distribution width reflects the variation in the size of circulating erythrocytes. After iron therapy the bone marrow begins producing new red blood cells (RBCs) so RDW initially increases then it starts to normalize as RBCs become more uniform in size. This may take several weeks to months to normalize [(8)].

The mean platelet volume represents the thrombocyte size. MPV may be elevated in IDA then it normalizes after iron therapy indicating the release of young, large, and active platelet to the circulation [(9)].

Serum ferritin is an indicator of total body iron stores, in the initial states of therapy it remains low. With iron therapy iron stores are replenished and serum ferritin is increased. Serum ferritin is essential marker for long term monitoring for iron therapy [(10)].

Evaluating these parameters for monitoring response to oral iron therapy is needed to adjust treatment and optimizing management of IDA.

Received: 23/10/2024
Accepted: 24/12/2024

Therefore, this study aimed to determine the demographic, clinical, and laboratory indicators for the response to oral iron therapy in Egyptian children with iron deficiency anemia.

PATIENTS AND METHODS

This cross-sectional study was conducted at Helwan University Hospital in Badr City, Egypt, on a convenient sample of 48 Egyptian children with IDA aged 1-7 years. Participants were recruited from the project "Screening of Anemia, Obesity, and Undernutrition in Children aged 1-7 years at Badr City", which was funded by Helwan University (11) the study eas conducted between November 2021 and to September 2022.

Iron deficiency anemia was diagnosed according to the following criteria: hemoglobin level below 11 gram (gm) % in children under 5 and below 11.5% for ages above 5 years [(12)] and MCV below -2SD for age related reference range (MCV below 70 fl for ages below 2 years, below 75 fl for ages between 2 – 6 years, and below 77 fl for ages above 6 years [(13)].

Children with IDA received oral iron (ferrous sulfate) in a daily dose of 6 mg/kg/day elemental iron for 3 months. Follow up visit was advised for blood testing after two weeks. Children with IDA who showed increased hemoglobin level at follow up were included in our study.

Children were classified to good responders if Hb level raised more than > 1 gm, and partial responders if below < 1 gm within the duration of oral iron (2-12 w) [(14)].

Patients were excluded from the study if they had any chronic disease or received blood transfusion in the last 4 months. All patients were subjected to a detailed history taking with emphasizing on nutritional history during infancy.

A thorough clinical examination was done, including:

- General examination with special emphasis on signs of anemia and vitamin deficiencies, e.g., pallor, nail spooning, mucositis, acro-orificial rash, alopecia and signs of chronic disease, e.g., jaundice, edema, clubbing, and purpura.
- Anthropometric measurements: weight was measured by a scale and height with a stadiometer, weight (Kg) divided by the height (meters square) was used to calculate body mass index (BMI). The Z scores for the anthropometric measures were calculated online using Canadian Pediatric endocrine group [(15)] and children were categorized according to the international classification of malnutrition [(16)].
- System examination: cardiac, respiratory, and abdominal examination to exclude undiagnosed chronic asymptomatic diseases.

Laboratory investigations included from the patient files, complete blood counts (Sysmex KX-21N, Sysmex Corporation, Japan), i.e., Hb level, MCV, RDW, MPV and serum ferritin (Beckman coulter Access 2) levels before and after iron therapy.

Severity of anemia was classified to [(17)]:

- Mild anemia when hemoglobin level between 10-10.9 g/dL, in children with ages below 5 years and between 11– 11.4g/dL for ages above 5 years.
- Moderate when hemoglobin level between 7– 9.9 g/dL, in children with ages below 5 years and between 8– 10.9 g/dL for ages above 5 years.
- Severe anemia when hemoglobin level below 7 g/dL in children with ages below 5 years and below 8 g/dL for ages above 5 years.

Compliance to oral iron (by questioning parents): as the child takes the correct amount, regularly without missing doses over a specified period as prescribed by the healthcare provider [(18)].

Ethics approval and consent to participate:
Written informed consent was obtained from the parents/legal guardians of all patients after explaining the nature, steps, and purpose of the study. The study was approved by the Faculty of Medicine, Helwan University Research ethics committee, and the confidentiality of patients' data was respected. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis: All data were collected and tabulated then analyzed statistically using IBM SPSS Statistics,Version 23. Quantitative data were presented as the mean ± SD and median (range), and qualitative data were presented as number and (percentage). For normally distributed quantitative data, the student t-test was used to compare between two groups, while Mann Whitney U test was used for non-normally distributed variables. Chi^2 test was used to compare qualitative variables. All tests were two sided. The level of significance was accepted when $P \leq 0.05$.

RESULTS

The characteristic data of the study group are shown in table 1. Among our studied children, 27% of their mothers received iron and vitamin supplements during pregnancy. About 69% of children were exclusively breastfed for four to 12 months. About 19% received formula in addition to breastfeeding, 2% received cow`s milk with breastfeeding, while 10.5% received formula. About 29% had pallor, two% had nails spooning, and 2 % had signs of rickets. About 30 (62.5%) of included children at baseline had mild anemia while 18 (37.5%) had moderate anemia.

The median duration of oral iron therapy was three weeks (IQR 2-4). About 52% of children were compliant with oral iron therapy while 48% were not compliant with their daily doses.

Table (1): The characteristic Data of the Study Group (N=48).

Variable	Values
Baseline Age in years: • Mean ± SD • Min - max	3.2 ± 1.4 (1.2 - 7)
Gender; N (%) • Male • Female	25 (52) 23 (48)
Residency; N (%) • *Badr* • *Urban*	48 (100) 48 (100)
Weight Z score: • Median (IQR) • Underweight; N (%)	-0.8 (-1.5 - -0.1) 9 (18.8)
Height Z score: • Median (IQR) • Short stature; short without undernutrition; N (%) • Stunting; short stature and underweight; N (%)	-1.04 (-1.8 - -0.2) 11 (22.9) 6 (12.5)
BMI Z score: • Median (IQR) • Wasting; N (%) • Overweight; N (%) • Obesity; N (%)	-0.3 (-1.1 - 0.6) 6 (12.5) 3 (6.25) 1 (2.1)
Hemoglobin in g/dl	10.04 ± 0.9 (7.5 - 11.3)
MCV fl	67.7 ± 6.3 47 – 75
RDW%	14.6 ± 2.6 11.1 – 22.2
TLC1000/cmm	8.6 ± 3.1 3.3 - 17.2
PLT1000/cmm	420.7 ± 105.7 200 – 668
MPV fl	8.9 ± 1.1 7- 12
Ferritin ng/ml	8.3 ± 4.2 1.9 – 15

BMI: body mass index, IQR: interquartile range, Max: maximum, Min: minimum, N: number, MCV=mean corpuscular volume, MPV=mean platelet volume, Platelet=PLT, RBC=red blood cell, RDW=red cell distribution, SD= standard deviation, TLC=total leucocyte count.

Comparison between baseline and follow-up anthropometric measures and laboratory findings in the study group are shown in table 2. Two children missed the anthropometric measures assessment at follow-up. No observed difference of significance between frequencies of underweight, stunting, wasting, and overweight or obesity was found at follows up.

Table (2): Comparison between Baseline and Follow-Up Anthropometric Measures and Laboratory Findings in the Study Group.

Variable	Baseline N=48	Follow Up N=46	P value
Anthropometric Measures			
Weight in kg: Mean ± SD	13.1 ± 3.4	14.2 ± 3.6	0.131
Weight Z score: Median (IQR)	-0.4 (-1.9 - 0.2)	-0. (-1.4 - -0.2)	0.001*
Height in cm: Mean ± SD	91.2 ± 11.6	95.3 ± 11.8	0.093
Height Z score: Median (IQR)	-1.04(-1.8 - -0.2)	-0.96(-1.9 - 0.8)	0.001*
BMI: Mean ± SD	15.6 ± 2	15.3 ± 1.7	0.4
BMI Z score: Median (IQR)	-0.3 (-1.1 - 0.6)	-0.4 (-1.1 - 0.7)	0.4
Laboratory findings			
Hemoglobin in g/dl	10.04 ± 0.9	11.05 ± 0.98	<0.001*
RBCs million/µL	4.5 ± 0.4	4.7 ± 0.4	0.017*
MCH pg	22.4 ± 2.9	23.6 ± 2.7	<0.04*
HCT %	30.6 ± 2.6	31.8 ± 3.3	0.052
MCV fl	67.7 ± 6.3	68.3 ± 6.4	0.65
MCHC g/dl	32.8 ± 2.02	34.4 ± 2.7	<0.002*
RDW %	14.6 ± 2.6	13.4 ± 2.03	0.015*
TLC 1000/cmm	8.6 ± 3.1	8.2 ± 2.7	0.4
PLT 1000/cmm	414.7 ± 102.8	413.8 ± 101.5	0.9
MPV fl	8.9 ± 1.1	9.4 ± 0.9	0.018*
Ferritin ng/ml	8.3 ± 4.2	17.1 ± 8.9	<0.001*

BMI: body mass index, HCT=hematocrit, IQR: interquartile range, Max: maximum, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, MCV=mean corpuscular volume, Min= minimum, MPV=mean platelet volume, N= number, RBC=red blood cell, RDW=red cell distribution, SD= standard deviation, TLC=total leukocyte count.

Hemoglobin response to oral iron therapy in the study group is shown in figure (1). The Relation between hemoglobin response and duration of oral iron therapy is shown in figure (2).

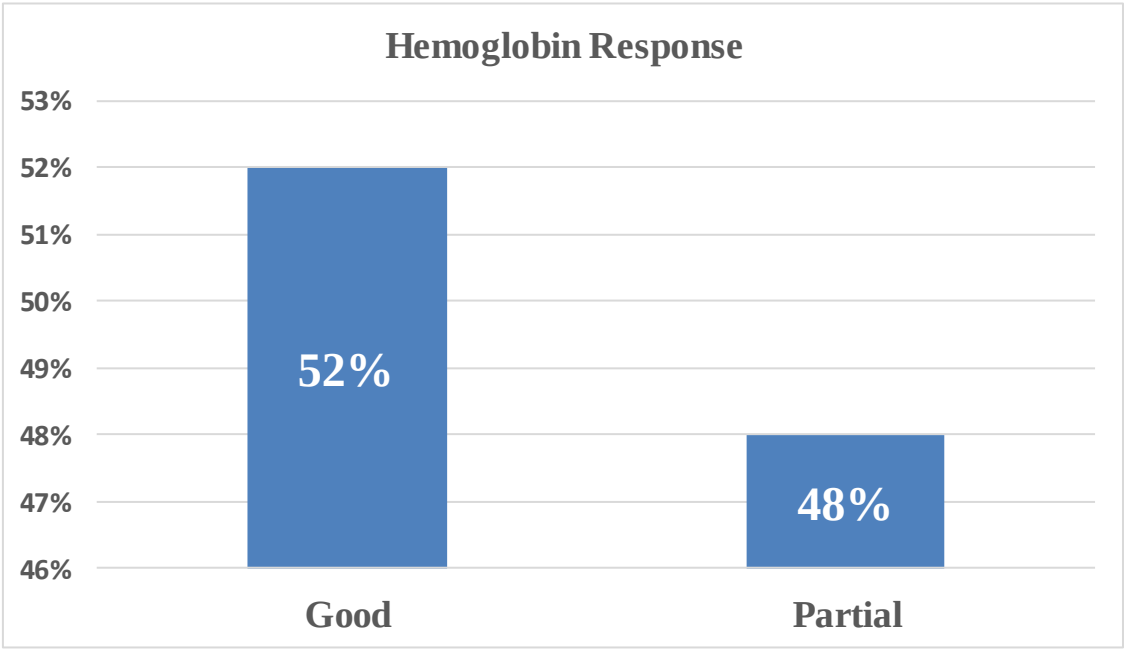

Figure (1): Hemoglobin Response to Oral Iron Therapy in the Study Group (N=48).

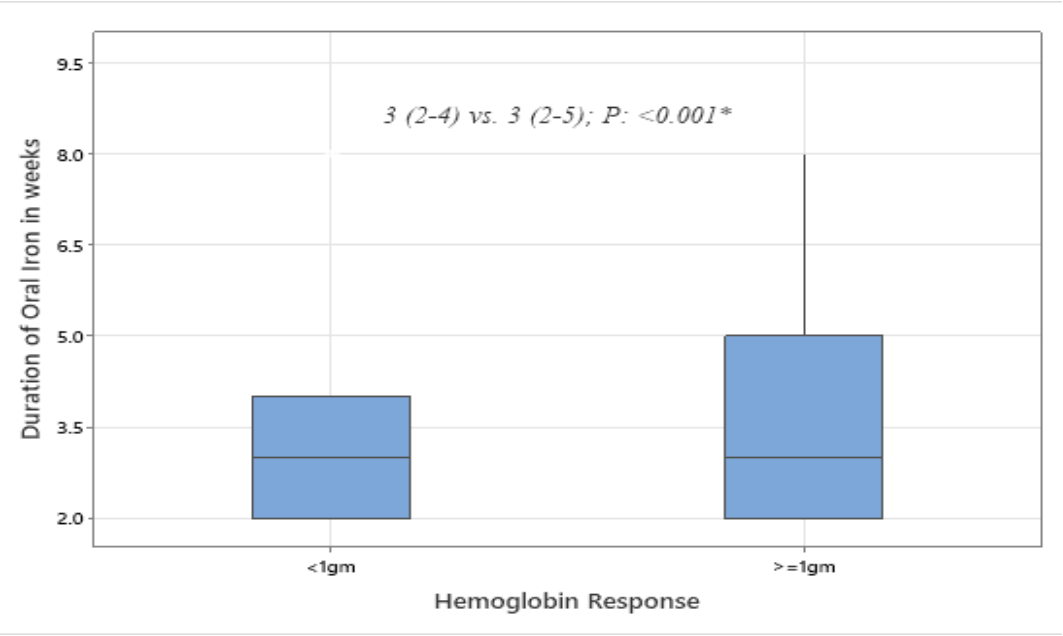

Figure (2): The Relation between Hemoglobin Response and Duration of Oral Iron Therapy (N=48). Data are presented as median (Interquartile range)

Comparisons between good and partial responders regarding different clinical and laboratory parameters are shown in table 3. We could not perform further advanced statistical analysis to test for specific indicators for iron response because no significant results were obtained from hematologic parameters.

Table 3: (N=48) Comparison between Good and Partial Responders Regarding Different Clinical and Laboratory Parameters.

HB Response	Partial (< 1 gm) N=23	Good (≥ 1 gm) N=25	P value
Severity of anemia at baseline: N (%) • Mild (30) • Moderate (18)	 16 (70) 7 (30)	 14 (56) 11 (44)	0.3
Compliance to treatment: N (%)	13 (56)	12 (48)	0.6
Boys **Girls**	13 10	12 13	0.6
Weight mean SD	13.1 ± 3.3	13.2 ± 3.5	0.8
Weight Z median **IQR**	-0.9 (–1.9- -0.37)	-0.7 (-1 - -1.3)	0.001*
Height mean SD	91± 10.3	91.9± 12.6	0.789
Height Z median **IQR**	-1.04 (-1.7- - 0.1)	-1.03 (-2 - -0.3)	0.001*
BMI Z median (IQR)	-0.23 (-0.9- 0.6)	-0.6 (-1.3- 0.7)	0.001*
RBCs million/µL	4.5 + 0.3	4.5 + 0.4	1
MCH pg	68.1 + 4.7	67.4 + 7.8	0.7
HCT %	30 + 2.5	31.2 + 2.5	0.1
MCV fl	22.4 + 2.7	22.4 + 3.2	1
MCHC g/dl	32.7 + 2.3	32.9 + 1.8	0.7
RDW %	14.2 + 2.5	15 + 2.7	0.3
TLC (10^9/L)	7.7 + 2.8	9.5 + 3.1	0.04*
PLT (×10^9/L)	398.7 + 94.4	445 + 114	0.1
MPV fl	8.8 + 1	8.9 + 1.2	0.6
Ferritin ng/ml	8.3 + 4	8.4 + 4.5	0.9

BMI: body mass index, HCT=hematocrit, IQR: interquartile range, Max=maximum, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, MCV=mean corpuscular volume, Min= minimum, MPV=mean platelet volume, N= number, RBC=red blood cell, RDW=red cell distribution, SD= standard deviation, TLC=total leucocyte count.

DISCUSSION

This was a cross-sectional study conducted at Helwan University Hospital in Badr City, on 48 children with IDA.

From our observation, the hemoglobin and hematocrit were significantly higher after the oral iron therapy compared to the base line. This was confirmed by several studies comparing hematological parameters before and after iron therapy. Similarly, **Russo *et al.*** [19], **Yuce *et al.*** [20], and **Das *et al.*** [21] in their studies among children with IDA reported a significant increase in Hb and hematocrit value after treatment with oral iron supplementation.

From our study, following oral iron therapy, the mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), values showed a significant increase, while the MCV values, showed no difference of significance. In comparison to our results, some studies reported a significant improvement in the hematological parameters including MCV, MCH and MCHC level after treatment with oral iron therapy [20-22].

In the current study, the mean RDW showed a significant decrease after the oral iron therapy. Similarly, **Korur *et al.*** [23] study on 50 patients with ID showed a significant decrease in RDW value after one month of treatment with iron therapy**.** The generation of RDW may be a good adjunct for the diagnosis of IDA. Different studies have reported that RDW can be used to distinguish between IDA and other causes of anemia such as thalassemia trait and anemia of chronic disease [24]. Contrary, **Ibrahim *et al.*** [25] conducted a study on 40 children with IDA, in Egypt, and they received elemental iron with a total daily dose of 6 mg/kg/day for 3 months. They reported that there was no significant difference in MCHC and RDW between before and after iron therapy.

In the present study, the MPV showed a significant increase, while the platelet count showed no difference of significance following oral iron therapy. As iron is an important cofactor for platelet synthesis, IDA is associated with thrombocytosis and micro platelet due to low iron [26]**.** Similarly to our result, **Faraj *et al.*** [9] showed a significant increase in the MPV value after iron treatment among 51 patients with IDA. Also, **Deshmukh *et al.*** [27] reported that hematological parameters were significantly altered in the study cases after one month of iron therapy including MPV. Other studies also showed that the mean MPV was significantly higher, while the platelet count was significantly decreased after oral iron therapy [20,22]**.** On the other hand, **Kurt and Demirkiran** [28] showed no change in MPV levels before and after iron therapy among patients with IDA.

In the present study, serum ferritin after treatment with oral iron therapy was significantly increased. Similarly, **Pachuta *et al.*** [29] showed a significant increase in serum ferritin levels after 3 weeks of oral iron therapy. In addition, **Ibrahim *et al.*** [25] reported that the Hb levels and serum ferritin of the studied cases were significantly higher after iron treatment than the base line.

From our findings, about 52% of children were good responders to oral iron therapy while about 48% of children were partial responders. The response is considered good if hemoglobin increased more than > 1 gm, and considered partial if below < 1 gm within the duration of oral iron (2-12). Similarly, **Patil *et al.*** [30] reported that the usual rate of increase in the hemoglobin level is about ≥1 g/dL within 14 days of oral iron.

From our study, the good responders had longer duration of iron therapy than partial responders. Also, **Andersen *et al.*** [31] concluded that longer duration of iron and moderate to high-dose of oral iron therapy was more effective at improving hemoglobin, ferritin, and iron deficiency anemia. The response to iron therapy differs according to the degree of anemia, moderate and severe anemia responds rapidly. Also, the duration of iron therapy might correlate with improved outcomes [17, 32]**.**

In the current study, there was no hematological parameter that can predict response to oral iron therapy. Pediatric studies reported different hematological markers as predictors to iron response therapy. Study showed that RDW can predict response to iron therapy [23]. Another study, reported that MPV can be considered as marker that helps in diagnosing IDA and for follow-up [9]**.**

This difference may be attributed to our small sample size; some of our cases were not compliant with their daily doses and there was no definite period for follow-up visits and patients were coming when they could come.

The current study had some limitations, first of which was not all children were compliant to oral iron therapy nor were compliant for follow up visits. Second, most of our cases had moderate and mild anemia and no children had severe degree of anemia.

CONCLUSION

The study revealed that the longer duration of oral iron therapy was associated with good response to therapy (> 1 gm). The hemoglobin, RBCs, MCH, HCT, MCHC, MPV and ferritin values showed a significant increase following oral iron therapy, while RDW values showed a significant decrease. In our results there was no laboratory parameter that can predict the response to oral iron therapy. Also, there was significant change in leucocytes between partial and good responders to iron therapy. There was a significant increase in weight and height of children after iron therapy.

Conflicts of Interest: Regarding the publishing of this paper, the authors state that they have no conflicts of interest.

Funding: This research was funded by Helwan University through the activity of the project "Screening of Anemia, Obesity, and Undernutrition in Children Aged 1-5 Years at Badr City".

REFERENCES

1. **World Health Organization (2015):** The Global Prevalence of Anaemia in 2011 . https://iris.who.int/handle/10665/177094
2. **Stoltzfus J (2003):** Iron deficiency: global prevalence and consequences. Food Nutr Bull., 24(4): S99-103. doi: 10.1177/15648265030244S206.
3. **Sekartini R (2021):** The importance of iron to support optimum cognitive development. World Nutr J., 5(S1):25–32. doi:10.25220/WNJ.V05.S1.0004
4. **Short W, Domagalski E (2013):** Iron deficiency anemia: evaluation and management. Am Fam Physician, 15;87(2):98-104. PMID: 23317073.
5. **Chaber R, Helwich E, Lauterbach R *et al.* (2024):** Diagnosis and treatment of iron deficiency and iron deficiency anemia in children and adolescents : Recommendations of the Polish Pediatric Society, the Polish Society of Pediatric Oncology and Hematology , the Polish Society of Neonatology , and the. Nutr Protoc., 16(21):3623. doi.org/10.3390/nu16213623.
6. **Mantadakis E, Chatzimichael E, Zikidou P (2020):** Iron deficiency anemia in children residing in high and low-income countries: Risk factors, prevention, diagnosis and therapy. Mediterr J Hematol Infect Dis., 1;12(1):e2020041. doi: 10.4084/MJHID.2020.041.
7. **Thomas W, Hinchliffe F, Briggs C *et al.* (2013):** Guideline for the laboratory diagnosis of functional iron deficiency. Br J Haematol., 161(5):639–48. doi: 10.1111/bjh.12311.
8. **Animasahun A, Itiola Y (2021):** Iron deficiency and iron deficiency anaemia in children : physiology, epidemiology, aetiology, clinical effects, laboratory diagnosis and treatment: literature review. J Xiangya Med., 6:1–14.
9. **Faraj A, Al-rubae M, Ansaf I (2021):** Evaluation of mean platelet volume before and after iron deficiency anemia treatment. Int J Pharm Res., 13(1):465-69. DOI:10.31838/ijpr/2021.13.01.081.
10. **World Health Organization (2020):** Serum ferritin concentrations for the assessment of iron status in individuals and populations: technical brief: World Health Organization. https://www.who.int/publications/i/item/9789240008526.
11. **Fouad M, Yousef A, Afifi A *et al.* (2023):** Prevalence of malnutrition & anemia in preschool children ; a single center study. Ital J Pediatr., 49(1):75. doi: 10.1186/s13052-023-01476-x.
12. **Brugnara C, Oski J, Nathan G (2009):** Nathan and Oski's hematology of infancy and childhood. 7th ed. Philadelphia: Saunders; p. 456.
13. **Fish D, Lipton M, Lanzkowsky P (2022):** Appendix 1- Hematological reference values. In: Lanzkowsky's Manual of Pediatric Hematology and Oncology. 7th ed. Academic Press, p. 767–80.
14. **World Health Organization (2017):** Nutritional anemias: tools for effective prevention and control. Geneva: World Health Organization. https://www.who.int/publications/i/item/9789241513067
15. **Canadian Pediatric endocrine group (CPEG), the official Canadian association for pediatric endocrinology (2018):** Z-score calculators. At: https://apps. cpeg- gcep. net.
16. **Cashin K, Oot L (2018):** Guide to anthropometry: a practical tool for program planners, managers, and implementers. Food and Nutrition Technical Assistance III Project, (FANTA)/ FHI., https://www.fantaproject.org/sites/default/files/resources/FANTA-Anthropometry-Guide-May2018.pdf
17. **Chandra J, Dewan P, Kumar P *et al.* (2022):** Diagnosis, treatment and prevention of nutritional anemia in children: Recommendations of the Joint Committee of Pediatric Hematology-Oncology Chapter and Pediatric and Adolescent Nutrition Society of the Indian Academy of Pediatrics. Indian Pediatr., 59(10):782–801. DOI: 10.1007/s13312-022-2622-2.
18. **Osterberg L, Blaschke T (2005):** Adherence to medication. N Engl J Med., 353(5):487–497. doi: 10.1056/NEJMra050100.
19. **Russo G, Guardabasso V, Romano F *et al.* (2020):** Monitoring oral iron therapy in children with iron deficiency anemia: an observational, prospective, multicenter study of AIEOP patients (Associazione Italiana Emato-Oncologia Pediatrica). Ann Hematol., 99 (3):413-20. doi: 10.1007/s00277-020-03906-w.
20. **Yuce S, Cure C, Cure E *et al.* (2015):** Evaluation of mean platelet volume before and after iron deficiency anemia treatment. Sifa Medical Journal, 2(1):7. DOI:10.4103/2148-7731.145794.
21. **Das I, Saha K, Mukhopadhyay D *et al.* (2014):** Impact of iron deficiency anemia on cell-mediated and humoral immunity in children: A case control study. Journal of Natural Science, Biology, and Medicine, 5(1):158.
22. **Miri-Aliabad G, Teiimouri A, Soleimanzadeh Mousavi H (2021):** Platelet parameters in children with iron deficiency anemia before and after treatment. International Journal of Pediatrics, 9(3):13249-13256. doi: 10.22038/ijp.2020.53642.4251
23. **Korur A, Açık Y, Solmaz S *et al.* (2019):** A novel parameter for predicting therapeutic response in iron deficiency anemia: Red blood cell distribution width. Euras J Fam Med., 8(3):107-12. doi.org/10.33880/ejfm.2019080303
24. **Aydogan G, Keskin S, Akici F *et al.* (2019):** Causes of hypochromic microcytic anemia in children and evaluation of laboratory parameters in the differentiation. J Pediatr Hematol Oncol., 41(4):e221-e223. doi: 10.1097/MPH.0000000000001382.
25. **Ibrahim A, Atef A, Magdy I *et al.* (2017):** Iron therapy and anthropometry: A case-control study among iron deficient preschool children. Egyptian Pediatric Association Gazette, 65(3):95-100. doi:10.1016/j.epag.2017.07.001.
26. **Brissot E, Troadec B, Loréal O *et al.* (2021):** Iron and platelets: A subtle, under-recognized relationship. Am J Hematol., 96(8):1008-1016. doi: 10.1002/ajh.26189.
27. **Deshmukh V, Konsam V, Gupta A *et al.* (2021):** Significance of platelet parameters in cases of iron deficiency anemia with reference to thromboembolic complications-A study in central India. Saudi Journal for Health Sciences, 10(3): 165-169.

28. **Kurt H, Demirkiran D (2023):** The effect of iron deficiency anaemia treatment on mean platelet volume. Ir J Med Sci., 192(4):1763-1767. doi: 10.1007/s11845-022-03221-5.
29. **Pachuta Węgier L, Kubiak M, Liebert A *et al.* (2020):** Ferrous sulfate oral solution in young children with iron deficiency anemia: An open-label trial of efficacy, safety, and acceptability. Pediatr Int., 62(7):820-27. doi: 10.1111/ped.14237.
30. **Patil P, Geevarghese P, Khaire P *et al.* (2019):** Comparison of therapeutic efficacy of ferrous ascorbate and iron polymaltose complex in iron deficiency anemia in children: A randomized controlled trial. Indian J Pediatr., 86(12):1112-1117. doi: 10.1007/s12098-019-03068-2.
31. **Andersen T, Marsden M, Duggan P *et al.* (2023):** Oral iron supplementation and anaemia in children according to schedule, duration, dose and cosupplementation: a systematic review and meta-analysis of 129 randomised trials. BMJ Glob Health, 8(2):e010745. doi: 10.1136/bmjgh-2022-010745.
32. **Yar S, Afridi K, Khan A *et al.* (2023):** Oral iron treatment for children with nutritional anaemia and factors that affect the results. Pakistan Journal of Medical & Health Sciences, 17:667-68. doi.org/10.53350/pjmhs2023172667.