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Original research article

COMPARATIVE EFFICACY OF FERROUS SULPHATE MONOTHERAPY VERSUS COMBINATION THERAPY WITH VITAMIN C IN PEDIATRIC IRON DEFICIENCY ANEMIA: A RANDOMIZED CONTROLLED TRIAL

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Abstract: *Iron deficiency is the single most common cause of anaemia worldwide. Treatment consists of improved nutrition and oral, intramuscular, or intravenous iron administration.* ***Objective:*** *To compare the outcome of monotherapy with ferrous sulphate and combination therapy with ferrous sulphate and vitamin C in children with iron deficiency anaemia.* ***Methods****: This randomised controlled trial was conducted in the Department of Pediatric Medicine, The Children's Hospital and The Institute of Child Health (CH&ICH), Multan, over six months from January 20, 2022, to July 20, 2023. A total of 166 children with iron deficiency anaemia were included in the study. Participants were randomly assigned to two groups: Group A received ferrous sulphate 5 mg/kg/day Fe^{2+} orally on an empty stomach plus vitamin C 6.3 mg/kg/day, while Group B received ferrous sulphate without additional vitamin C. Baseline and post-treatment measurements of haemoglobin, serum ferritin, and mean corpuscular volume (MCV) were taken. Data were analysed using SPSS-20, applying descriptive statistics and Student's t-test for comparison, with a significance level set at $p \leq 0.05$.* ***Results:*** *Of the 166 children, 111 (66.9%) were male, and 55 (33.1%) were female. The mean age was 24.55 ± 16.23 months. Rural residents accounted for 67 (40.4%), and urban residents were 99 (59.6%). Socioeconomically, 100 (60.2%) were from poor backgrounds, and 66 (39.8%) were middle-income. Among the mothers, 81 (48.8%) were illiterate, and 85 (51.2%) were literate. Post-treatment mean haemoglobin levels increased from 11.95 ± 1.02 g/dL to 12.74 ± 0.83 g/dL, serum ferritin levels from 30.73 ± 4.29 ng/mL to 32.87 ± 4.80 ng/mL, and MCV from 70.36 ± 3.81 fL to 74.49 ± 3.59 fL.* ***Conclusion:*** *Combination therapy with ferrous sulphate and vitamin C in pediatric patients with iron deficiency anaemia is well-tolerated and results in significant clinical improvement with minimal adverse reactions. This approach should be considered to enhance clinical outcomes, reduce morbidity, improve quality of life, and decrease healthcare costs.*

Keywords: Anemia, Combination Therapy, Ferrous Sulfate, Iron Deficiency, Pediatrics, Vitamin C

Introduction

Childhood is a critical stage of development, and early childhood caries are the most prevalent disease during this phase. They are often accompanied by significant comorbidities that impact children, their families, the community, and the healthcare system. Iron deficiency (ID) is the most common nutritional deficiency globally and poses a significant public health challenge, especially in developing countries. (1). Although precise data on the global prevalence of iron deficiency is lacking, it is estimated that most preschool children and pregnant women in developing countries are affected, with at least 30-40% of individuals in developed countries experiencing ID when anaemia is used as an indirect indicator. (2). According to 2001 World Health Organization (WHO) data, 30% of children aged 0 to 4 years and 48% of children aged 5 to 14 years are anaemic in developing countries. (3). In Pakistan, the prevalence of iron deficiency anaemia (IDA) in children has been reported to range between 15.2% and 62.5% across various studies. (4).

Anaemia is a crucial indicator of iron deficiency, leading to the interchangeable use of the ID of the term and IDA. However, iron deficiency can develop without anaemia, affecting tissues. Iron deficiency progresses through different stages. (5). Initially, reduced iron intake leads to depleted iron stores without affecting haemoglobin levels, resulting in iron deficiency without anaemia (6). During this stage, plasma ferritin levels and plasma transferrin saturation decrease. Prolonged negative iron balance eventually lowers haemoglobin levels, leading to IDA. (7). Thus, reduced body iron stores are classified as ID, and anemia due to worsening iron deficiency is classified as IDA.

Vitamin C supplementation enhances iron absorption, although its effect is relatively minor for individuals with balanced diets. Ferrous ascorbate has been shown to increase haemoglobin levels compared to colloidal iron in children. significantly (8). Studies have primarily focused on the effect of vitamin C on ferrous sulfate absorption, especially in meals containing iron absorption inhibitors. (9). A study in Turkey by Aycicek et al. reported that after 45 days of therapy, the serum haemoglobin level was 12 ± 1.4 g/dL in the ferrous sulfate group and 11.6 ± 1.9 g/dL in the ferrous sulfate and vitamin C group. The mean MCV was 73 ± 3 fL and 73 ± 5 fL, respectively, and serum ferritin levels were 31 ± 18 ng/mL in the ferrous sulfate group and 22 ± 23 ng/mL in the vitamin C group. Another study reported a mean Hb level of 9.98 ± 1.36 g/dL and a mean MCV of 69.19 ± 8.62 fL (10).

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Iron deficiency anemia is prevalent in developing countries. A thorough literature review on Google Scholar, PubMed, and PakMediNet revealed only one relevant study from Turkey, which compared the efficacy of vitamin C combination therapy. Due to the lack of local and international data and the absence of similar studies in Pakistan, we aim to conduct this study in our local population. The results will assist clinicians in treating these patients more effectively, improving their prognosis, quality of life, and productivity. Documenting the efficacy of combination therapy will aid in properly managing these children, contributing to a healthier pediatric population.

Methodology

This randomised controlled trial was conducted in the Department of Pediatric Medicine at The Children's Hospital and The Institute of Child Health (CH&ICH), Multan, over six months from January 20, 2022, to July 20, 2023. The study aimed to compare the effectiveness of Ferrous Sulphate with and without additional Vitamin C supplementation in children with iron deficiency anemia. The sample size was calculated using Epi-info software, resulting in 166 participants, with 83 children assigned to each group. Participants were selected using non-probability consecutive sampling.

The study included children aged 6 months to 12 years with iron deficiency anemia, a disease duration of more than two weeks, and consent from parents. Exclusion criteria included a history of iron supplementation therapy in the past six months, other known causes of anaemia (such as Thalassemia, Sickle cell anaemia, sideroblastic anaemia, G6PD deficiency, and hemolytic anaemia), and conditions like cerebral palsy, febrile seizures, and epilepsy.

Data collection involved a structured proforma to record findings. Participants meeting the inclusion and exclusion criteria were enrolled from the Pediatric Medicine department. Institutional Ethical Committee approval and informed consent from parents were obtained. Baseline investigations, including Hb, MCV, and serum ferritin levels, were conducted for all participants. The children were then randomly divided into two groups: Group A received Ferrous Sulphate (5 mg/kg/day) and Vitamin C (6.3 mg/kg/day) orally on an empty stomach. At the same time, Group B received only Ferrous Sulphate without additional Vitamin C. The treatment duration was six weeks, after which blood samples were taken to assess the therapy's outcomes. A senior pathologist with a minimum of five years of postgraduate experience conducted these tests.

Data were entered and analysed using SPSS-20. Descriptive statistics calculated means and standard deviations for age, Hb level, disease duration, MCV, MCHC, and serum ferritin levels. Frequencies and percentages were determined for categorical variables like gender, age groups, socioeconomic status, residential status (rural/urban), and maternal educational status. Student's t-test was used to compare Hb, MCV, and serum ferritin levels before and after therapy, with a significance level set at 0.05. To control for potential confounding variables, such as age, residential status, gender, disease duration, maternal education, and socioeconomic status, stratified tables were created. Post-stratification t-tests were applied to assess the impact of these factors on the outcomes, considering a p-value of ≤ 0.05 as significant.

Results

Our study comprised 166 patients meeting the inclusion criteria. Of these, 111 (66.9%) were male, and 55 (33.1%) were female (Table 1). The mean age was 24.55 ± 16.23 months, ranging from 6 to 72 months. The mean age for male patients was 26.77 ± 18.11 months, while for female patients, it was 20.09 ± 10.33 months (p=0.012). Most patients (144, 86.7%) were aged up to 5 years (Table 2).

Table 1: Gender Distribution

Gender	Total (n=166)	Group A (n=83)	Group B (n=83)
Male	111 (66.9%)	57 (68.7%)	54 (65.1%)
Female	55 (33.1%)	26 (31.3%)	29 (34.9%)

Table 2 Age Distribution

Age Group	Total (n=166)	Group A (n=83)	Group B (n=83)
Up to 5 years	144 (86.7%)	73 (88.0%)	71 (85.5%)
More than 5 years	22 (13.3%)	10 (12.0%)	12 (14.5%)

In our study, we analysed the residential status and socioeconomic background of the 166 patients. Most of the patients, 99 (59.6%), resided in urban areas, while 67 (40.4%) came from rural areas. When split into Group A and Group B, the distribution was pretty even, with urban patients constituting 60.2% of Group A and 59.0% of Group B, and rural patients making up 39.8% of Group A and 41.0% of Group B. Regarding socioeconomic status, 100 patients (60.2%) were from poor backgrounds, evenly distributed between the two groups. Middle-income patients accounted for 66 (39.8%), equally split between the groups (Table 3). The literacy status of the patients' mothers was also examined. Out of the 166 patients, 85 (51.2%) had literate mothers, while 81 (48.8%) had illiterate mothers. This distribution was nearly equal between the two groups, with Group A having 50.6% of mothers literate and 49.4% illiterate, and Group B having 51.8% literate and 48.2% illiterate Table 4.

This table summarises the clinical outcomes in terms of hemoglobin (Hb), serum ferritin levels, and mean corpuscular volume (MCV) between Group A and Group B. Group A showed significantly higher mean levels of hemoglobin (12.74 ± 0.83) compared to Group B (11.95 ± 1.02), with a p-value of 0.001. Serum ferritin levels were also higher in Group A (32.87 ± 4.80) than in Group B (30.73 ± 4.29), with a p-value of 0.004. Similarly, MCV was higher in Group A (74.49 ± 3.59) than in Group B (70.36 ± 3.81), with a p-value of 0.001. These differences highlight

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the better clinical parameters in Group A compared to Group B (Table 5). Hemoglobin levels were further stratified by gender, age, residential status, socioeconomic status, maternal literacy, and disease duration. Across all these categories, Group A consistently exhibited higher mean haemoglobin levels compared to Group B, with statistically significant p-values (all ≤ 0.003). For instance, male patients in Group A had a mean haemoglobin level of 12.75 ± 0.82, significantly higher than 11.88 ± 1.07 in Group B (p=0.001). Similarly, patients under 5 years in Group A had higher mean haemoglobin (12.71 ± 0.84) compared to those in Group B (11.90 ± 1.02, p=0.002) (Table 6). Serum ferritin levels also showed significant stratified differences between Group A and Group B across various demographics. Male patients in Group A had higher mean serum ferritin levels (31.99 ± 5.23) than Group B (29.85 ± 4.34, p=0.004). Female patients showed similar trends with Group A at 33.12 ± 4.24 versus Group B at 30.78 ± 4.87 (p=0.002). Age-wise, younger patients (up to 5 years) in Group A had higher mean serum ferritin (32.08 ± 5.13) than those in Group B (29.98 ± 4.12, p=0.003). These trends were consistent across residential status, socioeconomic background, maternal literacy, and disease duration, indicating better iron stores in Group A across all examined factors (Table 7**).**

Table 3 Residential Status and Socioeconomic Background

Characteristic	Total (n=166)	Group A (n=83)	Group B (n=83)
Rural	67 (40.4%)	33 (39.8%)	34 (41.0%)
Urban	99 (59.6%)	50 (60.2%)	49 (59.0%)
Poor	100 (60.2%)	50 (60.2%)	50 (60.2%)
Middle Income	66 (39.8%)	33 (39.8%)	33 (39.8%)
Illiterate Mothers	81 (48.8%)	41 (49.4%)	40 (48.2%)
Literate Mothers	85 (51.2%)	42 (50.6%)	43 (51.8%)

Table 4 Hemoglobin, Serum Ferritin, and MCV Levels

Parameter	Group A Mean ± SD	Group B Mean ± SD	p-value
Haemoglobin	12.74 ± 0.83	11.95 ± 1.02	0.001
Serum Ferritin	32.87 ± 4.80	30.73 ± 4.29	0.004
MCV	74.49 ± 3.59	70.36 ± 3.81	0.001

Table 5 Stratification of Hemoglobin Levels

Stratification	Group A Mean ± SD	Group B Mean ± SD	p-value
Male	12.75 ± 0.82	11.88 ± 1.07	0.001
Female	12.73 ± 0.81	11.94 ± 0.99	0.003
Up to 5 Years	12.71 ± 0.84	11.90 ± 1.02	0.002
More than 5 Years	12.76 ± 0.80	11.99 ± 1.01	0.001
Rural	12.65 ± 0.91	11.95 ± 1.03	0.001
Urban	12.60 ± 0.83	11.88 ± 1.03	0.001
Poor	12.80 ± 0.84	11.97 ± 1.01	0.001
Middle Income	12.86 ± 0.86	11.70 ± 0.98	0.001
Illiterate Mothers	12.86 ± 0.78	11.99 ± 0.99	0.001
Literate Mothers	12.82 ± 0.89	11.85 ± 1.06	0.001
Disease Duration ≤6m	12.80 ± 0.78	11.99 ± 0.98	0.001
Disease Duration >6m	12.85 ± 0.87	11.78 ± 1.01	0.001

Table 6 Stratification of Serum Ferritin Levels

Stratification	Group A Mean ± SD	Group B Mean ± SD	p-value
Male	31.99 ± 5.23	29.85 ± 4.34	0.004
Female	33.12 ± 4.24	30.78 ± 4.87	0.002
Up to 5 Years	32.08 ± 5.13	29.98 ± 4.12	0.003
More than 5 Years	33.15 ± 4.17	30.66 ± 4.97	0.002
Rural	32.11 ± 4.21	30.01 ± 4.09	0.002
Urban	32.99 ± 3.80	30.74 ± 3.98	0.002
Poor	31.89 ± 4.25	30.23 ± 4.11	0.002
Middle Income	33.09 ± 4.03	30.90 ± 4.22	0.002
Illiterate Mothers	31.95 ± 5.12	29.81 ± 4.19	0.001
Literate Mothers	33.56 ± 4.14	30.64 ± 4.72	0.002
Disease Duration ≤6m	32.94 ± 4.67	30.82 ± 4.34	0.001
Disease Duration >6m	33.08 ± 3.99	30.92 ± 3.86	0.001

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Table 7 Stratification of MCV Levels

Stratification	Group A Mean ± SD	Group B Mean ± SD	p-value
Male	75.01 ± 4.21	69.68 ± 3.98	0.001
Female	74.34 ± 3.89	70.79 ± 3.67	0.001
Up to 5 Years	74.56 ± 3.67	70.21 ± 3.91	0.001
More than 5 Years	74.21 ± 3.96	70.43 ± 3.82	0.001
Rural	74.21 ± 4.12	70.32 ± 3.81	0.001
Urban	74.43 ± 3.97	70.12 ± 3.98	0.001
Poor	74.71 ± 4.02	70.12 ± 3.80	0.001
Middle Income	74.22 ± 3.97	70.43 ± 3.82	0.001
Illiterate Mothers	74.34 ± 3.87	70.43 ± 3.55	0.001
Literate Mothers	74.21 ± 3.97	70.54 ± 3.61	0.001
Disease Duration ≤6m	74.23 ± 3.89	70.11 ± 3	0.001

Discussion

Iron deficiency anemia is a significant global health issue affecting children, women, and the elderly. It often coexists with various medical conditions. The causes of iron deficiency anaemia are multifaceted, including decreased iron intake and absorption, increased demand, and loss. Multiple causes are often present in a single patient. (11). While symptoms may be nonspecific, emerging evidence highlights the negative impact of iron deficiency anaemia on clinical outcomes in various medical conditions. Raising awareness about the prevalence and consequences of iron deficiency anaemia can facilitate early detection and management. (12). Diagnosis is typically straightforward with haemoglobin and serum ferritin measurements, although chronic inflammatory conditions may require higher ferritin thresholds and transferrin saturation evaluation for accurate diagnosis. (13). Both oral and intravenous iron supplements are available, with several patients and disease-related factors influencing management decisions. Iron deficiency anemia results from an imbalance between iron intake, storage, and loss, impacting erythrocyte production. Although rarely fatal, the health impact is considerable. The disease is easily diagnosed and treated in developed countries but is often overlooked by physicians. Conversely, it poses a significant health problem in underdeveloped regions, particularly among women and children (14). Effective prevention and treatment strategies are insufficient globally, especially among underprivileged populations.

Iron fortification remains a cornerstone in treating and preventing iron deficiency anemia. Menstruating and pregnant women, along with their children, are the most at-risk groups (15). In developing countries, iron is often provided with other micronutrients to reduce anaemia in schoolchildren. Home-based food preparations with iron supplements offer an alternative to industrial-scale supplementation of grains or commercial food products. Numerous oral formulations and dosing regimens are available for menstruating and pregnant women. Recently, intravenous iron formulations with improved safety profiles have been used to reduce transfusion needs in cases requiring rapid therapy (16). Given the large amount of iron provided intravenously, careful dosing is essential to prevent iatrogenic iron overload. Treatment should continue until anaemia is resolved and iron stores are replenished, indicated by normal hematocrit and serum ferritin levels of 50–100 µg/L.

In our study, we included 166 patients who met the inclusion criteria. Among these, 111 (66.9%) were male, and 55 (33.1%) were female. Malik et al., Mahmood et al., and Ziaullah et al. reported similar male predominance. Crary et al. and Mantadakis et al. reported different gender distributions, with Mantadakis et al. finding equal distribution. The mean age of our patients was 24.55 ± 16.23 months, with males averaging 26.77 ± 18.11 months and females 20.09 ± 10.33 months (p=0.012). Most patients (144 or 86.7%) were under five years old. Comparable age distributions were reported by Mahmood et al. and Ziaullah et al., while Crary et al. and Mantadakis et al. found higher mean ages (17-21).

Regarding residence, 67 (40.4%) were from rural areas and 99 (59.6%) from urban areas. Socioeconomically, 100 (60.2%) were from poor backgrounds, and 66 (39.8%) were middle-income. Mothers' education levels were evenly split, with 81 (48.8%) illiterate and 85 (51.2%) literate, similar to Mahmood et al.'s findings. The mean disease duration was 5.23 ± 4.34 months, with 105 (63.3%) having a duration of up to six months. Baseline haemoglobin, serum ferritin, and MCV levels were 12.74 ± 0.83 g/dL, 32.87 ± 4.80 ng/mL, and 74.49 ± 3.59 fL, respectively, compared to 11.95 ± 1.02 g/dL, 30.73 ± 4.29 ng/mL, and 70.36 ± 3.81 fL after treatment. These findings are consistent with those of Aycicek et al., who reported similar haemoglobin, MCV, and serum ferritin levels after treatment (10).

The study's limitations include small sample size and single-centre design, limiting generalizability. The six-week follow-up may not capture long-term effects, and exclusion criteria may restrict applicability to severe cases. Variations in compliance, lack of dietary data, and lack of blinding introduce potential bias. Socioeconomic factors were noted but not explored, and the study only focused on oral supplementation, neglecting other methods and broader outcomes.

Conclusion

In conclusion, our study suggests that combining ferrous sulphate with vitamin C in pediatric patients with iron deficiency anemia is well-tolerated and yields positive clinical results with minimal adverse reactions. This

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combination therapy significantly improved haemoglobin levels, serum ferritin levels, and MCV. Clinicians should consider using this combination therapy to achieve desired clinical outcomes and reduce related morbidities. This approach will enhance patients' quality of life and reduce healthcare-related costs.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department concerned. (IRB-NMC-120-Dated 12-06-2022)
Consent for publication
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Conflict of interest
The authors declared an absence of conflict of interest.

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References

1. Saleem MK, Sattar K, Ejaz KF, Rehman MU, Saleem H, Khursheed S, et al. Use of telemedicine to tackle health problems in South Asia during the COVID-19 era and beyond a systematic review. Annals of Medicine and Surgery. 2024;86(2):1012-20.
2. Greffeuille V, Fortin S, Gibson R, Rohner F, Williams A, Young MF, et al. Associations between zinc and hemoglobin concentrations in preschool children and women of reproductive age: an analysis of representative survey data from the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) Project. The Journal of Nutrition. 2021;151(5):1277-85.
3. Turawa E, Awotiwon O, Dhansay MA, Cois A, Labadarios D, Bradshaw D, et al. Prevalence of anaemia, iron deficiency, and iron deficiency anaemia in women of reproductive age and children under 5 years of age in south africa (1997–2021): A systematic review. International Journal of Environmental Research and Public Health. 2021;18(23):12799.
4. Monisha S. To Study the Prevalence of Anemia in Antenatal Patients attending OPD in a Tertiary Care Centre: Madras Medical College, Chennai; 2022.
5. Camaschella C, Girelli D. The changing landscape of iron deficiency. Molecular Aspects of Medicine. 2020;75:100861.
6. Al-Naseem A, Sallam A, Choudhury S, Thachil J. Iron deficiency without anaemia: a diagnosis that matters. Clinical Medicine. 2021;21(2):107.
7. Romano AD, Paglia A, Bellanti F, Villani R, Sangineto M, Vendemiale G, et al. Molecular aspects and treatment of iron deficiency in the elderly. International Journal of Molecular Sciences. 2020;21(11):3821.
8. Shubham K, Anukiruthika T, Dutta S, Kashyap A, Moses JA, Anandharamakrishnan C. Iron deficiency anemia: A comprehensive review on iron absorption, bioavailability and emerging food fortification approaches. Trends in Food Science & Technology. 2020;99:58-75.
9. Basrowi RW, Dilantika C. Optimizing iron adequacy and absorption to prevent iron deficiency anemia: the role of combination of fortified iron and vitamin C. World Nutrition Journal. 2021;5(S1):33-9.
10. Aycicek A. Ferrous Sulfate Versus Ferrous Fumarate Plus Zinc Sulfate and Vitamin C for Treatment of Iron Deficiency Anemia in Children. Glob J Hematol Blood Transfus. 2015;2:15-9.
11. Rakanita Y, Sinuraya RK, Suradji EW, Suwantika AA, Syamsunarno MRA, Abdulah R. The Challenges in Eradication of Iron Deficiency Anemia in Developing Countries. Systematic Reviews in Pharmacy. 2020;11(5).
12. Albaroudi IN, Khodder M, Al Saadi T, Turk T, Youssef LA. Prevalence, diagnosis, and management of iron deficiency and iron deficiency anemia among Syrian children in a major outpatient center in Damascus, Syria. Avicenna Journal of Medicine. 2018;8(03):92-103.
13. Svenson N, Bailey J, Durairaj S, Dempsey-Hibbert N. A simplified diagnostic pathway for the differential diagnosis of iron deficiency anaemia and anaemia of chronic disease. International Journal of Laboratory Hematology. 2021;43(6):1644-52.
14. Bendavid E, Boerma T, Akseer N, Langer A, Malembaka EB, Okiro EA, et al. The effects of armed conflict on the health of women and children. The Lancet. 2021;397(10273):522-32.
15. Tunkara-Bah H. Hepcidin-guided screen-and-treat for iron-deficiency anaemia in young children. The Lancet Global Health. 2023;11(1):e12-e3.
16. Ivanovska V, Rademaker CM, van Dijk L, Mantel-Teeuwisse AK. Pediatric drug formulations: a review of challenges and progress. Pediatrics. 2014;134(2):361-72.
17. Malik NA, Shah SA, Mashhadi SF. EVALUATION OF INJECTABLE IRON SUCROSE THERAPY IN CHILDREN WITH IRON DEFICIENCY ANEMIA: Injectable Iron Sucrose in Iron Deficiency Anemia. Pakistan Armed Forces Medical Journal. 2016;66(5):680-83.
18. Mahmood A, Ahmed P, Altaf C, Aziz S, Azim W. Clinicohaematological features of iron deficiency anemia in children between 1-5 years of age. Pakistan Journal of Pathology. 2006;17(3).
19. Ziaullah K, Nawaz S, Shah S, Talat A. Iron deficiency anemia as a cause of breath holding spells. Journal of Postgraduate Medical Institute. 2005;19(2).
20. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. Pediatric blood & cancer. 2011;56(4):615-9.
21. Roganovic J, Mantadakis E. Parenteral iron therapy in children with iron deficiency anemia. World J Pediatr. 2016;12(1):122.

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