ORIGINAL ARTICLE

COMPARISON OF IRON ALONE VERSUS IRON COMBINED WITH VITAMIN A FOR MANAGING IRON DEFICIENCY ANAEMIA

Sadia Mir, Attia Bano*, Hina Batool Siddiqui, Nasreen Ali***, Noor-e-Sahar†, Madiha Noor††**

Department of Paediatrics, Rawal Institute of Health Sciences, Islamabad, *THQ Hospital Kahuta Rawalpindi, **PAC Hospital Kamra/Attock, ***PAF Hospital, Islamabad, †THQ Hospital Hazro, Attock, ††Medical Squadron, PAF Base Nur Khan, Rawalpindi, Pakistan

Background: Iron deficiency is the most prevalent nutritional deficiency and a significant global public health concern. This study aims to rapidly reduce the prevalence of iron deficiency anaemia (IDA) and prevent related cognitive impairments in children. Objective was to compare the effectiveness of iron alone versus iron combined with Vitamin-A in reducing iron deficiency anaemia in children (aged 6–59 months of age). **Methods:** This randomized controlled trial over 6 months conducted in Department of Paediatrics, PAC Hospital, Kamra. Study included 104 children (52 in each group), aged 6–59 months, of either gender, with haemoglobin levels below 11 g/dL and serum ferritin levels below 12 ng/mL. Participants were randomly assigned to two groups: Group A received iron plus Vitamin A, while Group B received only iron therapy. After three months, patients were assessed for changes in haemoglobin concentration and ferritin levels as ferritin stores replenish in specified period. Data were recorded using a specially designed form. **Results:** In Group A, the mean age was 37±7.10 months, and in Group B, it was 40±6.25 months. In Group A, 27 (52%) children experienced a reduction in IDA, and in Group B, 15 (29%) children showed a reduction in IDA. Older children in Group A and those having literate mothers showed better improvement in IDA in Group A. **Conclusion:** Combining iron with Vitamin A is more effective than iron alone in reducing iron deficiency anaemia in children.

Keywords: Iron plus Vitamin A, Iron therapy, Iron Deficiency Anaemia, IDA

Pak J Physiol 2025;21(1):41–4, **DOI:** https://doi.org/10.69656/pjp.v21i1.1752

INTRODUCTION

Iron deficiency Anaemia (IDA) is a widespread nutritional problem and a significant global health concern.[1–3] It has an incidence of 39% between 0–4 years of age and 48.1% between 5 and 14 years.[4] Nationwide, the rate of iron deficiency anaemia (IDA) in children varies from 15.3% to 62.5%.[5] High risk groups for IDA include infants, pre-schoolers, and women of reproductive age.[2]

IDA progresses in stages, starting with the depletion of iron reserves. It is marked by reduced serum ferritin, low mean corpuscular volume (MCV), and low mean corpuscular haemoglobin (MCH).[6] As iron stores become exhausted, decreased haemoglobin levels lead to anaemia. Common causes of IDA in children include inadequate dietary intake, excessive milk consumption during periods of rapid growth, low birth weight, worm infestations, and gastrointestinal losses. Symptoms may include loss of appetite, angular stomatitis, irritability, dysphagia, pica, and increased susceptibility to infections. Importantly, IDA can lead to cognitive impairments, particularly during first two years of life.[7,8]

Oral ferrous salts are a common treatment for IDA, but treatment often extends for 6 months to a year due to the slow increase in haemoglobin concentration and ferritin stores. Challenges such as poor compliance, lengthy treatment duration, altered bowel habits, disrupted iron absorption, and ineffective counselling can hinder outcomes. Given the magnitude of the problem and the limited effectiveness of prolonged oral iron therapy, new interventions are needed to rapidly increase haemoglobin levels and reduce the duration of IDA treatment.[9,10]

Studies suggest that combining iron with Vitamin A supplements is more effective than iron alone in treating IDA.[11] This effectiveness is attributed to Vitamin A's role in enhancing iron absorption, metabolism, and erythropoiesis.[12] Besides Vitamin A is also related to concentrations of IGF type 1 (Insulin like growth factor), that helps to mobilize body iron stores.[1] A study in Malaysia showed that children receiving Vitamin A supplements experienced a more significant increase in haemoglobin levels after three months compared to those who did not receive Vitamin A. The treatment group also saw a notable reduction in IDA prevalence (22.4%) compared to the control group (5.6%).[13]

This study aims to rapidly decrease IDA prevalence to mitigate long-term cognitive impairments in children. Another study at Brazil revealed that Vitamin A supplementation is a safeguarding tool against anaemia and stunting especially in underdeveloped countries.[1,2]

METHODOLOGY

This controlled trial was conducted from 1 Oct 2023 to 1 Apr 2024, at the Outpatient Department of Paediatrics,

Pakistan Aeronautical Complex, Kamra. A sample size of 104 was calculated by G*Power calculator, with 52 children in each group, achieving 80% power with a 5% significance level. The expected reduction in IDA after three months of treatment was 22.4% for the iron plus Vitamin A group and 5.6% for the iron-only group.[14]

Children aged 6 to 59 months, of either gender, presenting with haemoglobin levels below 11 g/dL and serum ferritin levels below 12 ng/mL, were included. Children with co morbidities (congenital heart disease, celiac disease, Thalassemia Major, inflammatory bowel disease, malabsorption syndromes, chronic diarrhoea, haemorrhoids, and bleeding disorders) and infectious diseases (pneumonia, otitis media, liver diseases) were excluded from study. All children were ensured to be on healthy diet according to their age, they were also de-wormed before starting the treatment.

The study was performed only on patients whose parents agreed to their participation and approved to the informed consent. Demographic variables (name, age, and gender) were recorded. Children were randomly assigned to two groups: Group A received iron plus Vitamin A, while Group B received only iron. Vitamin A was administered at a dose of 500 IU three times a week for three months. Both groups were treated with iron supplements in the form of ferrous salts for three months. Follow-up was conducted in the outpatient department every 2 weeks to ensure compliance and address issues regarding availability of medicines and any side effect. After three months, patients were evaluated for changes in haemoglobin and ferritin levels by blood samples to assess the reduction in IDA. At the time of sampling it was ensured that patients are not suffering acutely from any illness as it may alter the ferritin results.

Data were entered and analysed using SPSS-20. Quantitative variables like age, haemoglobin concentration, and ferritin levels were presented as means with standard deviations. Qualitative variables such as gender and reduction in IDA were presented as frequencies and percentages. Chi-square tests were used for comparing IDA reduction between groups, with $p \leq 0.05$ considered significant. Stratification controlled for age, gender, and maternal education.

Children who failed to respond to oral iron therapy were investigated for other disorders like celiac disease, Thalassemia syndromes, Megaloblastic anaemia, worm infestations, H pylori gastritis and inflammatory bowel disease. After ruling out these disorders, the candidates were considered for intravenous iron therapy.[9] Although it was an infrequent option in the past, but now with availability of new iron products, it allows for better replacement of total iron deficit. The new products are safe and approved by FDA like iron sucrose therapy.[10]

RESULTS

Mean age of children in Group A was 37±7.10 months, 16 (31%) children were aged 6–30 months, and 36 (69%) were aged 31–59 months. Mean age of children in Group B was 40.0±6.95 months, 17 (33%) children were aged 6–30 months, and 35 (67%) were aged 31–59 months. Group A had 21 (40%) males and 31 (60%) females, while Group B had 23 (44%) males and 29 (56%) females. In Group A, 19 (37%) children weighed ≤10 Kg and 33 (63%) weighed >10 Kg, with a mean weight 12±3.56 Kg. In Group B, 20 (38%) children weighed ≤10 Kg and 32 (62%) weighed >10 Kg, with a mean weight 13±4.19 Kg. Eighteen mothers of Group A children were 'literate' while 34 were 'illiterate'. Twenty mothers of Group B children were 'literate' and 32 were 'illiterate'. (Table-1).

Group A showed more significant improvements compared to Group B in serum haemoglobin and ferritin levels. Pre-treatment, both groups had similar values. Post-treatment, Group A had a significantly higher increase both in haemoglobin (2.72 g/dL *vs* 0.63 g/dL) and ferritin (3.46 ng/mL *vs* 1.71 ng/mL) (p=0.0001) (Table-2, 3).

In Group A, 27 (52%) children showed a reduction in IDA compared to Group B with 15 (29%) only (p=0.016) (Table-4). Overall, the addition of Vitamin A to iron treatment proved more effective in improving iron status and reducing IDA.

Maternal education played a significant role in our patients' treatment. It was easy for us to make them follow medical advice and to ensure timely medical care in case of complications. Reduction in IDA among the two groups was also stratified by age, gender, and maternal education. Older children in Group A and those having literate mothers showed better improvement in IDA in Group A. (Table-5).

Table-1: Basic demographics

Variables	Group A	Group B
Age (Months)		
6–30	16 (31.0%)	17 (33.0%)
31–59	36 (69.0%)	35 (67.0%)
Mean±SD	37.0±7.10	40.0±6.95
Gender		
Male	21 (40.0%)	23 (44.0%)
Female	31 (60.0%)	29 (56.0%)
Weight (Kg)		
≤10 Kg	19 (37.0%)	20 (38.0%)
>10 Kg	33 (63.0%)	32 (62.0%)
Mean±SD	12±3.56	13±4.19
Mother's education		
Educated	18 (35.0%)	20 (38.0%)
Uneducated	34 (65.0%)	32 (62.0%)

Table-2: Serum haemoglobin concentration (g/dL)

Haemoglobin Level	Group A	Group B	*p*
Pre treatment	6.09±2.24	6.28± 2.10	0.6564
Post treatment	8.8±1.76	6.91±1.88	0.0001
Rise in Hb level	2.72±0.48	0.63±0.22	0.0001

Table-3: Serum ferritin level (ng/mL)

Serum Ferritin Level	Group A	Group B	*p*
Pre treatment	8.31±3.47	8.11±2.94	0.7518
Post treatment	11.77±2.51	9.82±2.64	0.0002
Rise in Hb level	3.46 ±0.96	1.71±0.30	0.0001

Table-4: Reduction in IDA [n (%)]

Reduction in IDA	Group A	Group B
Yes	27 (52%)	15 (29%)
No	25 (48%)	37 (71%)

Table-5: Stratification of reduction in IDA with variables

Variables	Reduction	Group A	Group B	*p*
Age				
6–30 months	Yes	8	5	0.2263
	No	8	12	
31–59 months	Yes	19	10	0.0380
	No	17	25	
Gender				
Male	Yes	11	7	0.1391
	No	10	16	
Female	Yes	16	8	0.0576
	No	15	21	
Mothers' education				
Educated	Yes	9	6	0.2078
	No	9	14	
Uneducated	Yes	18	9	0.0404
	No	16	23	

DISCUSSION

Our study was focused to imply the effects of Iron therapy with and without Vitamin A supplementation in managing iron deficiency anaemia. The results from this study revealed that adding Vitamin A to iron considerably improved the haemoglobin and ferritin levels along with overall improvement in Iron deficiency anaemia in children. Furthermore maternal education was also found to be an important contributing factor in establishing better compliance to therapy and improved consequences.

One of the major results in our research was the noteworthy improvement in both serum haemoglobin and ferritin in patients who received iron plus Vitamin A (Group A) in comparison to those who received Iron therapy alone (Group B). The mean rise in haemoglobin level in Group A was 2.72 g/dL notably higher than 0.63 g/dL increase noted in Group B (p<0.0001).This data lines up many studies in recent years that have also shown synergistic effects of Vitamin A on Iron absorption & metabolism, improving anaemia.[14,15] Vitamin A is also believed to improve gut absorption of iron Vitamin A has been shown to improve the intestinal absorption of iron, that also leads to improved response in Group A patients.[16]

On the other-hand in Group B that only received iron therapy, a smaller increase in haemoglobin and ferritin levels were observed. This emphasizes the tentative limitation 0f iron alone to improve anaemia especially in children who have concurrent deficiencies of other micro-nutrients as well like vitamin A. previous studies have also shown similar results that isolated iron treatment may be less efficient in improving anaemia in areas where multiple micro-deficiencies prevalent.[17]

One more essential finding of our study was the higher rate of iron deficiency anaemia reduction in Group A, i.e., 52% as compared to Group B, i.e., 29% (p=0.016). This study supports the design that Vitamin A can magnify the efficacy of iron therapy in managing Nutritional anaemia. A similar study was performed by Kumar *et al*, Implying that patients receiving combined iron and vitamin A had a higher resolution rate of iron deficiency anaemia than those receiving isolated iron.[18] This result is in harmony with the theory that vitamin A plays a vital role in enhancing iron usage, thereby improving anaemia.[19]

Recent data also reveals that micro-nutrient deficiencies like vitamin A and iron are very common in young population particularly in under developed countries and combined therapy may be more effective than dealing with individual deficiencies.[4] Our finding also supports the evidence of beneficial response of combined therapy thereby decreasing the national burden of Iron deficiency anaemia.

Out study highlights crucial role of maternal education in managing iron deficiency anaemia in children. Educated mothers are more likely to comply with treatment plans and seek early medical care. Educated mothers are better informed about the benefits of iron supplementation and fortification, and can recognize early symptoms of anaemia, leading to improved health outcomes for their children. Maternal education is a key component of public health programs aimed at reducing iron deficiency anaemia, particularly in young children.

The age range in our study was balanced enough between the two groups falling in range of 31 to 59 months. This is the most vulnerable group due to rapid growth, development and higher nutritional requirements. There was no considerable difference noted on the base of age or gender. However some studies did reveal a greater prevalence of iron deficiency anaemia in females due to menstrual blood loss. Gender was not contributing factor in our study but still a large sample may have helped us to give a better insight.

Al-Mekhlafi HM *et al* found that anaemia was more common in children aged 10 years or younger compared to those older than 10 years. There was no significant difference in the prevalence of anaemia between male and female children.[12]

Iron deficiency anaemia is a notable problem of our country. It is easily treatable by simple measures like iron supplementation, food fortification, and maternal awareness programs. A study conducted in Pakistan[8] revealed that the prevalence of IDA in Pakistani children represents a moderate burden on country economy. The

affected children more often belonged to mother having IDA and living in areas where food security is undermined. It requires both vertical and horizontal programs like iron supplementation and food fortification to alleviate the burden.

Although our study proved to be successful in establishing a role of iron and vitamin A but still there are some limitations to look upon. Our study duration was short and a long follow-up data would have been more helpful to establish that haemoglobin and ferritin levels remained consistent with time. Long follow-up would also be helpful to ensure better healthy lifestyle. A detailed study would also be useful to ponder on confounding factors like dietary pattern, iron stores, and presence of underlying conditions that influence therapy response.

CONCLUSION

Combining iron with Vitamin A is more effective than iron alone in reducing IDA. Children who fail to respond to iron treatment altogether should be evaluated for other underlying disorders. Emphasis on vertical and horizontal programs like iron supplementation and food fortification is required to alleviate the burden on national basis.

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Address for Correspondence:

Dr Hina Batool Siddiqui, Assistant Professor, Department of Paediatrics, PAF Hospital Kamra/Attock, Pakistan. **Cell:** +92-332-2033585

Email: hinairtaza14@gmail.com

Received: 1 Sep 2024 **Reviewed:** 21 Feb 2025 **Accepted:** 2 Mar 2025

Contribution of Authors:

SM: Drafting of work **AB:** Data collection **HBS:** Data analysis
NA: Data interpretation **NS:** Critical review **MN:** Statistical analysis

Conflict of interest: None
Funding: None