Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.69980/g0w6zk29

IMPACT OF IRON DEFICIENCY ANEMIA ON IMMUNE FUNCTION, INFECTION SUSCEPTIBILITY, AND THERAPEUTIC RESPONSE TO IRON SUPPLEMENTATION IN SCHOOL-AGE CHILDREN: A CLINIC-COMMUNITY BASED STUDY

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ABSTRACT

Background: Iron deficiency anemia (IDA) is the most common nutritional deficiency in children and is linked to reduced immune response and increased risk of infections. It has a wide range of consequences beyond blood disorders, including growth, development and health.

Objectives: To evaluate the impact of iron deficiency anemia on immune function, infection susceptibility, and therapeutic response to iron supplementation in school-age children.

Methods: This was a clinic-community based cross-sectional study, conducted at Pak International Medical College between January 2024 and January 2025. Seventy-two children between the ages of 6-14 years with iron deficiency anemia were recruited by non-probability consecutive sampling. Clinical, laboratory and demographic information was gathered. Blood indices, iron indices and immune indices (leukocyte count and immunoglobulin levels) were measured. The children were given oral iron supplements for three months, and changes were evaluated. Statistical analysis was performed using SPSS version 26 ($p \leq 0.05$) was considered significant.

Results: The mean age was 9.8 ± 2.1 years, with a male predominance (55.6%). Most children had moderate anemia (54.2%) and inadequate dietary iron intake (68.1%). Recurrent infections were observed in 66.7% of participants, predominantly respiratory infections. Significant alterations in immune parameters were noted. A strong association was found between anemia severity and infection frequency ($p < 0.001$). Following iron supplementation, significant improvements were observed in hemoglobin, ferritin, immune markers, and reduction in infection episodes ($p < 0.001$).

Conclusions: Iron deficiency anemia adversely affects immune function and increases infection susceptibility in children. Iron supplementation significantly improves both hematological and clinical outcomes, highlighting the importance of early detection and intervention.

Keywords: Iron deficiency anemia; Immune function; Infection susceptibility; Iron supplementation; School-age children; Hemoglobin; Serum ferritin; Immunoglobulins; Nutritional deficiency; Pediatric anemia.

INTRODUCTION

Iron deficiency anemia (IDA) remains a major public health concern worldwide, particularly in developing countries where nutritional deficiencies are prevalent among children. It has been estimated that a large number of school children are iron deficient, as a result of low dietary iron intake, impaired iron absorption and increased iron requirements during growth. While anemia is well known for its blood-related symptoms, its impact on immunity and risk of infections is now being recognized (1-3).Iron is essential for various physiological functions, such as oxygen transport, metabolism, and immune responses. It is required for the growth and differentiation of immune cells, such as lymphocytes, and the production of immune responses. Iron deficiency has been reported to affect both the innate and adaptive immune responses, resulting in decreased phagocytic function, changes in cytokine production, and reduced immunoglobulin synthesis. Consequently, children with IDA are more susceptible to infections, particularly respiratory and gastrointestinal infections (4-6).Beyond its impact on susceptibility to infection, iron deficiency anemia (IDA) also affects child development, with cognitive impairment, poor physical stamina, and school absenteeism. These outcomes have individual, social and economic implications. Despite its prevalence and health impacts, IDA remains poorly recognised and treated in many low- and middle-income countries (7-9).Iron supplementation is a safe and inexpensive treatment for IDA. Earlier research has shown increases in hemoglobin concentrations with supplementation, but results for effects on immune function and infection are inconsistent. Moreover, there is a lack of data from the local population that considers clinical, hematological and immunological indices in a clinic-community approach (10).Therefore, this study was conducted to evaluate the impact of iron deficiency anemia on immune function, infection susceptibility, and therapeutic response to iron supplementation in school-age children. The findings aim to provide evidence for strengthening early screening programs and targeted nutritional interventions to reduce the burden of IDA and its associated complications.

METHODOLOGY

This clinic-community based study was conducted to evaluate the impact of iron deficiency anemia on immune function, infection susceptibility, and therapeutic response to iron supplementation in school-age children. The study was carried out at Pak International Medical College and its affiliated community settings over a period of one year from January 2024 to January 2025 after obtaining institutional approval.In this study, 72 children between 6 and 14 years of age were recruited through a consecutive sampling method. Children from the outpatient department and community screening camps with clinical and laboratory diagnosis of iron deficiency anemia were enrolled. Iron deficiency anemia was defined as a hemoglobin concentration below the age-specific reference range, low serum ferritin and microcytic hypochromic indices. Children with chronic systemic disease, known hematological disease (such as thalassemia), recent blood transfusion, or current infections requiring hospital admission were excluded.Informed parental or guardian consent was obtained and demographic and clinical information was collected on a proforma. Data on age, gender, socioeconomic background, dietary patterns and history of recurrent infections were obtained. This included examination for pallor, anthropometry and nutritional assessment.Aseptic blood samples were obtained for baseline studies. Hematological indices such as hemoglobin, mean

corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) were determined using an automated blood cell counter. Serum iron indices were measured including serum ferritin, serum iron, total iron binding capacity (TIBC), and transferrin saturation. Immune status was assessed by total and differential leukocyte counts and immunoglobulin concentrations (IgG, IgM, and IgA). Serum ferritin and immunoglobulin concentrations were measured by enzyme-linked immunosorbent assay (ELISA).Children were given iron supplements orally as per the recommended dose (3-6 mg/kg/day of elemental iron) for three months. Adherence was assessed with follow-up visits and parental reporting. Follow-up assessments were performed to evaluate the impact on hematological indices, immune markers and infection rates.Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The paired t-test was used to compare pre- and post-treatment parameters, and the chi-square test was applied to assess associations between anemia severity and infection frequency. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The study was conducted on 72 school-going children. The average age was 9.8 ± 2.1 years, with a slight male bias. The majority of the children were from low socioeconomic status families and had low dietary iron intakes.

Table 1: Demographic and Baseline Characteristics

Variable	Category	n (%)
Age Group	6–8 years	24 (33.3%)
	9–11 years	30 (41.7%)
	12–14 years	18 (25.0%)
Gender	Male	40 (55.6%)
	Female	32 (44.4%)
Residence	Community	39 (54.2%)
	Clinic	33 (45.8%)
Socioeconomic Status	Low	46 (63.9%)
	Middle	26 (36.1%)
Nutritional Status	Underweight	38 (52.8%)
	Normal	34 (47.2%)
Dietary Iron Intake	Inadequate	49 (68.1%)
	Adequate	23 (31.9%)

Most children presented with classical symptoms of anemia, particularly pallor and fatigue. A high proportion reported recurrent infections, predominantly respiratory tract infections. School absenteeism was also common among affected children.

Table 2: Clinical Profile and Infection History

Variable	Category	n (%)
Pallor	Present	61 (84.7%)
Fatigue	Present	55 (76.4%)
Irritability	Present	42 (58.3%)
Recurrent Infections	Yes	48 (66.7%)
	No	24 (33.3%)
Type of Infection	Respiratory	34 (47.2%)
	Gastrointestinal	9 (12.5%)

	Skin	5 (6.9%)
Infection Frequency	≥3 episodes/6 months	41 (56.9%)
Antibiotic Use	Yes	44 (61.1%)
School Absenteeism	≥5 days/month	37 (51.4%)

The majority of children had moderate anemia, with significantly reduced hemoglobin and ferritin levels. Microcytic hypochromic indices were observed, consistent with iron deficiency anemia.

Table 3: Hematological Parameters

Parameter	Mean ± SD
Hemoglobin (g/dL)	8.9 ± 1.2
MCV (fL)	72.5 ± 6.8
MCH (pg)	23.1 ± 3.4
Serum Ferritin (ng/mL)	11.6 ± 4.2
Serum Iron (µg/dL)	38.4 ± 9.7
TIBC (µg/dL)	412.3 ± 35.6
Transferrin Saturation (%)	12.2 ± 3.1
RDW (%)	16.8 ± 2.4

Severity of Anemia

Severity	n (%)
Mild	14 (19.4%)
Moderate	39 (54.2%)
Severe	19 (26.4%)

Iron deficiency anemia in children was associated with immune dysfunction, including low lymphocyte numbers and high levels of inflammatory markers. Relative decrease in immunoglobulin levels indicated impaired adaptive immunity.

Table 4: Immune Function Parameters

Parameter	Mean ± SD
Total Leukocyte Count ($\times 10^9$/L)	6.8 ± 1.5
Neutrophils (%)	62.4 ± 7.1
Lymphocytes (%)	29.6 ± 6.3
NLR	2.1 ± 0.8
IgG (mg/dL)	820 ± 120
IgM (mg/dL)	88 ± 25
IgA (mg/dL)	95 ± 28

A statistically significant association was observed between anemia severity and infection frequency. Children with severe anemia had a higher frequency of recurrent infections compared to those with mild anemia (**$p < 0.001$**).

Table 5: Association between Anemia Severity and Infection Frequency

Anemia Severity	≥3 Infections n (%)	<3 Infections n (%)	p-value
Mild	5 (6.9%)	9 (12.5%)	
Moderate	21 (29.2%)	18 (25.0%)	
Severe	15 (20.8%)	4 (5.6%)	**<0.001**

Iron supplementation led to marked improvement in the hematological and immune response. Moreover, there was a significant decline in the incidence and severity of infection.

Table 6: Pre- and Post-Iron Supplementation Outcomes

Parameter	Pre-treatment	Post-treatment	p-value
Hemoglobin (g/dL)	8.9 ± 1.2	11.4 ± 1.1	<0.001
Serum Ferritin (ng/mL)	11.6 ± 4.2	28.7 ± 6.5	<0.001
MCV (fL)	72.5 ± 6.8	80.2 ± 5.4	<0.001
Infection Episodes	3.4 ± 1.2	1.6 ± 0.8	<0.001
School Absenteeism (days/month)	6.2 ± 2.1	2.8 ± 1.4	<0.001

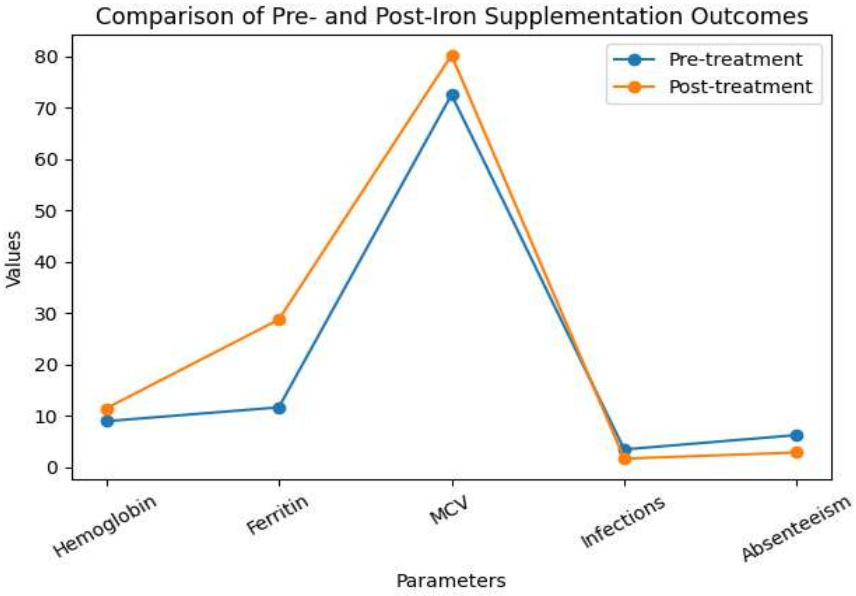


Figure 1: Comparison of hematological and clinical parameters before and after iron supplementation among school-age children. Significant improvement was observed in hemoglobin, ferritin, and MCV levels, along with a marked reduction in infection frequency and school absenteeism following treatment.

DISCUSSION

This clinic-community based study highlights the significant impact of iron deficiency anemia (IDA) on immune function, infection susceptibility, and response to iron supplementation among school-age children. The findings demonstrate that IDA is not only a hematological disorder but also has profound implications on immune competence and overall child health.In our study, most of the children were from low socioeconomic status and had poor dietary iron intake, which is in line with results from developing nations where malnutrition is still a big concern. The prevalence of underweight children also highlights the co-existence of malnutrition and micronutrient deficiencies. This is in line with recent studies in the region that reported inadequate dietary habits and low socioeconomic status are major factors contributing to childhood iron deficiency (11-14).Many study participants had moderate-to-severe anemia, microcytic hypochromic indices and low ferritin, indicating iron deficiency. These hematological indices have been well documented in children, suggesting that IDA remains the most prevalent nutritional deficiency globally. Crucially, our study goes beyond the hematological parameters by reporting changes in immune indices, such as low lymphocyte populations, and relatively low immunoglobulin levels, suggestive of impaired adaptive immunity (15, 16).This study found a link between IDA and susceptibility to infections. Severe anemia was associated with a greater incidence of infection, especially respiratory tract

infections. This may be due to iron's role in immune cell division, cytokine synthesis and mucosal integrity. IDA affects the innate and adaptive branch of the immune system, leading to increased frequency of infections. This result is consistent with recent reports that found a close association between iron deficiency and the immune response (17, 18).The other key finding was that anemic children have a higher consumption of antibiotics and absenteeism from school, highlighting the impact of IDA on health-related quality of life. Common infections and other illnesses not only impact physical health but also learning and quality of life. This suggests the importance of early diagnosis and treatment at individual and population level.Iron supplementation resulted in marked improvement in hematological indices such as ferritin, hemoglobin and red cell indices. More significantly, there was a significant decrease in the incidence of infection and improvement in the immune response. This study supports the therapeutic effects of iron supplementation not just for correcting anemia, but also for improving the immune response. These observations are consistent with the results of interventional studies, in which iron supplementation resulted in improved immune responses and lower morbidity in children (19, 20).However, there are some limitations to the study. The study was relatively small and restricted to one institution and associated community, which may limit the ability to extrapolate the results. Moreover, the study was limited in terms of assessing advanced immunological markers such as cytokine profiling, given the resources required. This study did not include follow-up to determine long-term outcomes.

CONCLUSION

Iron deficiency anemia significantly impairs immune function and increases susceptibility to infections in school-age children. Children with more severe anemia are at a higher risk of recurrent infections, increased antibiotic use, and school absenteeism. Iron supplementation leads to substantial improvement in hematological parameters, immune status, and clinical outcomes.

Early screening, nutritional interventions, and timely iron supplementation programs at both clinical and community levels are essential to reduce the burden of iron deficiency anemia and its associated complications. Future large-scale studies are recommended to further explore long-term immunological outcomes and optimize intervention strategies.

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