



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 a widespread nutritional disease among school-age children and may impair immune activity and predispose these children to infection.

Objective: To determine the effect of iron deficiency anemia on immune homeostasis, predisposition to infectious diseases, and immune response to iron replacement in school-aged children.

Methods: The current study is a cross-sectional study conducted in a clinic-community-based research at Northwest School of Medicine between January 2024 and January 2025. Eighty-two children between the ages of 5 and 12 years who were confirmed with IDA were recruited using consecutive sampling. Baseline demographic, clinical, and hematological information was gathered, such as hemoglobin, serum ferritin, and serum iron. The SPSS v25 version was used to analyze the data, Chi-square tests, and paired t-tests were performed, and $p \leq 0.05$ was taken as significant.

Results: Recurrent infections, mostly respiratory, were most common in most children, with low hemoglobin significantly linked to an increased frequency of infections ($p = 0.021$). Hemoglobin and ferritin levels ($p < 0.001$) and the number of infection episodes significantly improved with iron supplementation.

Conclusion: School-age children with iron deficiency anemia show decreased immune response and susceptibility to infections. Oral iron supplementation is effective in restoring hematological

parameters and decreasing infection burden, which implies the role of early identification and management of IDA with the help of combined clinic-community strategies.

Keywords: Iron deficiency anemia, children of school-going age, the immune system, and vulnerability to infections.

INTRODUCTION

Iron deficiency anemia (IDA) is still one of the most common nutritional diseases on an international scale, especially in children of low-and middle-income nations.[1] It is known to have low levels of hemoglobin as a result of insufficient availability of iron to transport oxygen, and cellular metabolism is impaired.[2] In addition to hematologic effects, iron deficiency has an extensive impact on various physiologic systems, particularly the immune system.[3] Iron is important in the growth and development of immune cells, such as lymphocytes, and in the production of reactive oxygen species that phagocytes utilize to combat pathogens.[4] As a result, iron deficiency may result in the inability to respond to infections adequately, both innate and adaptive.

The prevalence of IDA in school-going children is also very high globally. The World Health Organization estimates that about 30-40% of children aged 5-14 years have anemia, of which almost half are due to iron deficiency.[5] In South Asia, which includes Pakistan, the prevalence is even worse because of unhealthy dietary consumption, parasitic infections, and socioeconomic imbalance. The surveys conducted at the national level point out that a considerable percentage of school-aged Pakistani children are affected by anemia which adversely influences not only their physical but also their cognitive development, performance in school, and overall quality of life.[6]

Immune dysfunction is closely related to iron deficiency.[3] It suppresses cell-mediated immunity and the production of cytokines, and disrupts the activity of neutrophils and macrophages.[7] These changes lead to children being susceptible to frequent infections, mostly in the respiratory system, gastrointestinal diseases, and parasite infestations. Moreover, hypoxia due to anemia can further impair the host defense mechanisms.[3] Several studies have shown that children with IDA have more, worse, and longer infections than their non-anemic counterparts.[8, 9] Nevertheless, iron status and infection are not simple because iron is also needed to maintain the growth of microorganisms, and it is a question of when and whether iron supplementation should be applied to microorganism-prone populations.[10]

The treatment of the IDA has been based on therapeutic iron supplementation.[11] The use of oral iron therapy has been found to have a positive effect on iron stores and hemoglobin levels, but the effects of oral iron on immune responses and infection outcomes remain under study.[12] Some studies have reported increased immunity and decreased rates of infections after iron therapy, but some other studies have indicated the momentary increase of infection risk, especially in regions highly infected with infectious diseases.[13] These contradictions indicate that specific research needs to be conducted in different contexts in order to better understand the dual role of iron in host defense and pathogen growth.

Since iron deficiency anemia is so prevalent in school-age children and has so many broad-reaching effects on immune competence and susceptibility to infections, there is an urgent need to produce strong, locally appropriate evidence. Knowledge of how IDA affects immune functioning and predisposition to infections and the responses to iron supplementation of children in real-life conditions could inform more effective preventive public health and clinical interventions. A clinic-community-based strategy presents a special possibility of capturing the clinical parameters, as well as environmental determinants, to gain a comprehensive view. The current study will thus be aimed at bridging the knowledge gaps by evaluating, in detail, the effects of iron deficiency anemia on immune defenses, vulnerability to infections, and responses to iron supplementation in children aged enough to attend school. The current study aimed to evaluate the effects of iron deficiency anemia on immune response, vulnerability to infection, and response to iron supplementation in a group of school-age children in a clinic-community environment.

METHODOLOGY

It was a cross-sectional analytical study, and it was conducted as a clinic community-based study. The researchers conducted the study at the Northwest School of Medicine, which was done with the help of associated clinical and community-based settings, to be able to represent both hospital-going and community-based school-age kids. The period of the study was one year, between January 2024 and January 2025.

A sample size was determined through the openEpi software, considering a confidence level of 95% with a margin of error of 5 percent, and the prevalence rate of iron deficiency anemia among school-age children was estimated to be 36.8%.[14] The final sample size included in the study was 82 participants using the normal formula in OpenEpi to conduct prevalence studies.

A non-probability consecutive sampling method was used. Children were being included in the study, provided that they were aged between 5 and 12 years and were diagnosed with iron deficiency anemia through clinical assessment and laboratory tests such as hemoglobin levels and iron profile. Only children whose parents or guardians had given informed consent and were available to undergo a clinical evaluation as well as follow-up, were included in the study. Children were not included in the study when they had known chronic diseases, including chronic kidney disease, congenital heart disease, malignancy, hematological disorders other than iron deficiency anemia, including thalassemia or sickle cell anemia. The participants were also not allowed to take part in the study when they had had a blood transfusion in the last three months or when they were in an acute severe infection that would need hospitalization, or when their parents or guardians did not consent to participate in the research.

A pre-designed proforma was used to collect data. Eligible participants were enlisted after receiving ethical approval from the institutional review board and informed consent from parents/guardians. Demographic information such as age, gender, nutritional status, socioeconomic background, and educational status was taken as the baseline. Clinical assessment was done to evaluate signs and symptoms of anemia and the susceptibility to infection, including the history of recurrent respiratory tract and gastrointestinal infections, as well as other common diseases. To identify the iron deficiency anemia, laboratory tests comprised of complete blood count (CBC), serum ferritin, serum iron, and total iron binding capacity (TIBC). The immune activity was evaluated using the clinical measures of frequency and severity of infections.

The standard oral iron supplementation was administered to all the diagnosed patients of iron deficiency anemia as per the pediatric guidelines. There were follow-up assessments to determine the response to the therapy, such as the improvement in the hemoglobin levels and the decrease in the incidence of infections over time.

The data collected were all input and analyzed with version 25 of the Statistical Package of Social Sciences (SPSS). Mean and standard deviation (SD) were used to describe quantitative variables (age and hemoglobin levels), and frequencies and percentages were used to describe categorical variables (gender and frequency of infection and response to therapy). Comparative analysis was done to determine the relationship between iron deficiency anemia and susceptibility to infections. Categorical variables were chi-square tested, and a paired t-test or an independent t-test was applied to continuous variables where necessary. A p-value of below 0.05 was taken as significant.

RESULTS:

The study involved 82 school-age children. The population of the study was a group of children of a wide age range, with some slight dominance of older children. There was a sufficient representation of both genders with a slight predominance of males. The ratio of respondents to rural regions and less socioeconomic classes was greater and corresponds to the population most prone to nutritional deficiencies. Hematology screening revealed that all subjects had iron deficiency anemia, with low iron levels in the blood and empty iron stores in the form of serum ferritin and serum iron, and high iron binding capacity. (Table 1) Infection patterns were assessed, and a high percentage of children

were found to have recurring infections, which showed impaired immune functions. The most frequent clinical manifestations included respiratory tract infections, gastrointestinal infections, and mixed infections. The number of different infections among the participants differed, and a significant proportion reported several infections in the past several months, which might be related to heightened susceptibility to iron deficiency. (Table 2) Additional investigation proved that there was a strong correlation between the intensity of anemia and the rate of infections. The children who had lower hemoglobin were more likely to be infected on a number of occasions as opposed to those whose hemoglobin levels were relatively higher, pointing to the influence of iron status on immune competence (Table 3). After the iron supplementation, significant changes in the hematological parameters were noted. There was a great recovery in the levels of hemoglobin and iron stores, which means that there was a positive therapeutic response to oral iron therapy. Simultaneously, a significant reduction in the rate of infection had been reported following treatment, and it indicated recovery of immune capability, including iron deficiency remediation (Table 4). On the whole, most of the participants showed a favorable therapeutic response accompanied by a notable decline in the hematological response and infection load. Nevertheless, a lower percentage of respondents had moderate to poor responses, and this can be explained by the reality that there could be factors of poor nutrition, environmental, or compliance factors that influence the response (Table 5, Figures I and II).

Table 1: Baseline Characteristics and Hematological Profile (n = 82)

Variable	Frequency (n)	Percentage (%)	Mean $\pm$ SD
Age Group (years)			8.9 $\pm$ 2.1
5–8 years	34	41.5%	
9–12 years	48	58.5%	
Gender			
Male	46	56.1%	
Female	36	43.9%	
Residence			
Urban	37	45.1%	
Rural	45	54.9%	
Socioeconomic Status			
Low	49	59.8%	
Middle	25	30.5%	
High	8	9.7%	
Hemoglobin (g/dL)			9.1 $\pm$ 1.2
Serum Ferritin (ng/mL)			11.4 $\pm$ 3.6
Serum Iron (μg/dL)			38.7 $\pm$ 8.5
TIBC (μg/dL)			412.5 $\pm$ 35.2

Table 2: Infection Profile and Association with Hemoglobin Levels

Variable	Frequency (n)	Percentage (%)	p-value
Recurrent Infections			
Yes	56	68.3%	
No	26	31.7%	
Type of Infection			
Respiratory	38	46.3%	
Gastrointestinal	21	25.6%	
Mixed/Other	23	28.1%	
Infection Frequency (6 months)			
≤ 2 episodes	24	29.3%	
3–5 episodes	39	47.6%	

>5 episodes	19	23.2%	
Association with Hemoglobin			0.021

Table 3: Cross-tabulation of Hemoglobin Levels and Infection Frequency

Hemoglobin Level	≤2 Episodes	3–5 Episodes	>5 Episodes	Total
7–8.9 g/dL	6	18	14	38
9–11 g/dL	18	21	5	44
Total	24	39	19	82

Table 4: Therapeutic Response to Iron Supplementation (n = 82)

Parameter	Before Treatment (Mean ± SD)	After Treatment (Mean ± SD)	p-value
Hemoglobin (g/dL)	9.1 ± 1.2	11.3 ± 1.0	<0.001
Serum Ferritin (ng/mL)	11.4 ± 3.6	18.9 ± 4.2	<0.001

Table 5: Effect of Iron Therapy on Infection Frequency and Overall Response

Variable	Before Treatment n (%)	After Treatment n (%)
≤2 episodes	24 (29.3%)	51 (62.2%)
3–5 episodes	39 (47.6%)	23 (28.0%)
>5 episodes	19 (23.2%)	8 (9.8%)
Overall Response		
Good Response	52 (63.4%)	—
Moderate Response	21 (25.6%)	—
Poor Response	9 (11.0%)	—

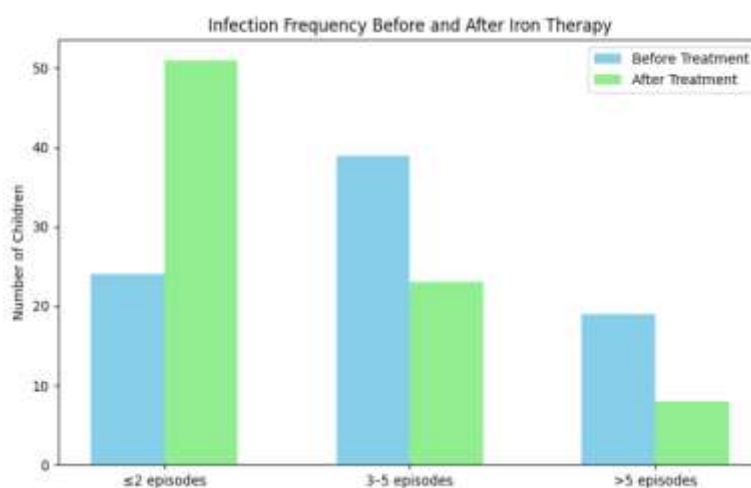


Figure I: A clustered bar chart showing the decrease in children with 3–5 and >5 episodes and the increase in those with ≤2 episodes after treatment.

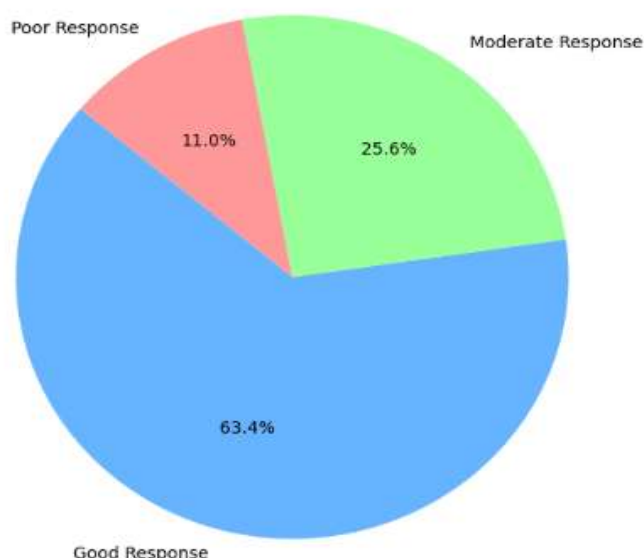


Figure II: A pie chart showing the proportion of children with good, moderate, and poor responses

DISCUSSION

The current clinic-Community-based research was used to determine the effect of iron deficiency anemia (IDA) on immune, infectious, and iron supplementation response in school-age children. The results showed that there was a high prevalence of recurrent infections, that there was a strong correlation between the level of anemia and the frequency of infection, and that there was a great improvement in hematological measures and infection resolution after iron therapy.

The children in this study were in lower socioeconomic groups, and they were moderately anaemic. These results are also supported by the study of Habib et al. (2023), which was based on the National Nutrition Survey and revealed that iron deficiency anemia is still very high among Pakistani children, but to a large extent is caused by nutritional deficiencies and infections.[15] This resemblance highlights the unremitting public disease load of IDA in developing nations and justifies the external validity of our outcomes.

One of the main findings of the current study was a very high percentage of children with frequent infections, in particular, respiratory tract infections. This is in line with those observed by Sonia et al. (2020), who have stated that iron deficiency anemia is closely linked with frequent respiratory infections in children because of compromised immune systems.[16] Similarly, Lee (2023) pointed out that iron deficiency impairs immune system regulation, resulting in high susceptibility to infection and inflammatory diseases.[17] These experiments confirm our observation that IDA is a major impairment of host immunity.

In addition, we showed that the relationship between low hemoglobin concentration and high infection rate between the two groups was statistically significant. The results are in line with the meta-analysis of Sulviani et al. (2023), who found that poor iron indices correlate with a higher predisposition to infection-related conditions in the child population.[18] The biological viability of this association has been well established because iron is an essential factor in the growth of immune cells, the production of cytokines, and the clearance of pathogens.

In terms of therapeutic outcomes, we reported a significant change in hemoglobin and serum ferritin levels after iron supplementation. The results are comparable to previous randomized and observational studies showing that iron treatment is effective in correcting hematological parameters. To illustrate, the reports assessing pediatric groups have continued to indicate that iron supplementation causes significant changes in both the hemoglobin and ferritin levels, which means that the iron stores are replenished.[19]

Significantly, a large decrease in the frequency of infections due to iron therapy was also noted in our study. Interventional studies have also supported this finding, as iron supplementation has been shown to not only increase iron status but also decrease morbidity, especially respiratory tract morbidity. Equally, the findings of even more recent studies on iron supplementation in children have demonstrated better clinical outcomes without the significant risk of increasing the risk of infections, making it apparent that the correction of iron deficiency boosts immune functions.[19]

Nevertheless, there is a complicated connection between iron supplementation and infection. A study by Abbas et al. (2022) has also indicated that augmented provision of iron can be a hypothetical stimulus to the growth of pathogens, especially gut microbiota.[20] This duality of iron poses a therapeutic dilemma, as it has been in other literature dealing with infections generally, since iron is key to the growth of a host immune response as well as to the growth of a microbe. Our results indicate, in spite of these fears, the net positive impact of iron supplements in enhancing immune performance in iron-deficient children.

Our results are mostly similar to those reported in the literature, as it is evident that the international community supports their claims and finds that IDA-related impaired immunity and higher risk of infection, and iron supplementation have hematological and clinical benefits. But as opposed to some studies where they indicated neutral or mixed effects on the outcome of the infection, our study indicated a definite decrease in the frequency of infection after treatment. This disparity can be explained by clinic-community design, more successful follow-up, or differences in baseline nutritional and environmental variables.

An additional noteworthy finding in our study was the fact that, despite the fact that most of the children displayed positive therapeutic response, a subgroup of children displayed less than ideal improvement. Much the same has been observed in other recent studies, where poor compliance, persistent infections, malnutrition, and underlying inflammation have been found to affect response to iron therapy. This underscores the importance of combined interventions that have a focus on nutritional and environmental determinants.

In general, the results of the current study are strong enough to support previous research and provide data that are locally specific to Pakistan, especially among school-age children, which is a relatively understudied population. The research is novel in that it addresses the immune functioning (through patterns of infection), hematology response, and treatment outcomes all through one framework.

There were some limitations of this study. The sample size ($n = 82$) could be considered relatively small, and non-probability consecutive sampling could be a source of the selection bias as well as a limitation of the generalizability of the results. Indirectly, immune functioning was measured by clinical measures, including the number of infections as opposed to measures of specific immunology, and this can minimize accuracy. Also, the use of the history of infection as reported by the caregivers creates a risk of bias in recall. The follow-up time was not long, and this did not provide an opportunity to assess long-term outcomes of the iron supplementation. The possible confounding variables that included the nutritional status, parasitic infections, environmental conditions, and compliance with treatment were not completely controlled, and this might have affected the observed associations.

CONCLUSION

The current research found that iron deficiency anemia has a severe effect on the immune system and predisposes school-age children to infections. The low hemoglobin levels were found to be strongly associated with the increased frequency of infection. The given iron supplementation resulted in a significant improvement of hematological parameters and a decrease in the infection burden, which proves the therapeutic effect of the intervention. The findings clarify the need to identify and treat iron deficiency anemia at an early age using integrated clinic-community interventions to enhance child health and minimise infection-related morbidity.

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