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Lower respiratory tract infection associated with iron deficiency anaemia

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Abstract

Background:
Lower respiratory tract infections (LRTIs) are a leading cause of childhood morbidity and mortality globally, particularly in low- and middle-income countries. Iron deficiency anaemia (IDA), a prevalent nutritional disorder in early childhood, impairs immune function and may increase susceptibility to respiratory infections. This study aimed to evaluate the association between IDA and LRTIs in children aged 1–5 years using objective haematological and biochemical markers.

Methods: A case-control study was conducted at a tertiary care hospital in Rawalpindi from January 2023 to June 2023, spanning a period of six months. Seventy children aged 1–5 years were enrolled, including 35 cases diagnosed with LRTI and 35 age-matched controls without respiratory illness. IDA was defined by haemoglobin <11 g/dL, MCV <75 fL, serum ferritin <30 ng/mL, and serum iron <50 µg/dL. Demographic and clinical data were recorded, and laboratory investigations were conducted. Associations were analysed using chi-square tests and odds ratios (OR), with significance set at $p \leq 0.05$.

Results: IDA was significantly more prevalent among LRTI cases (60.0%) than controls (22.9%) ($p = 0.002$), with an OR of 5.04 (95% CI: 1.77–14.36). Children with LRTI exhibited significantly lower mean haemoglobin (9.23 vs. 11.58 g/dL), MCV (68.5 vs. 76.3 fL), serum ferritin (21.4 vs. 41.8 ng/mL), and serum iron (36.6 vs. 74.9 µg/dL) compared to controls (all $p < 0.001$). The association between IDA and LRTI persisted across age, gender, and socioeconomic strata and was strongest among children from lower-income households.

Conclusion: IDA is significantly associated with an increased risk of LRTIs in young children, with affected individuals being five times more likely to develop these infections. Routine screening and early correction of iron deficiency, particularly in socioeconomically disadvantaged populations, may reduce the incidence and severity of respiratory infections in early childhood. These findings support the integration of nutritional interventions into child health and infection prevention strategies.

Keywords: Iron deficiency anaemia, lower respiratory tract infections, children, immune function, case-control study, serum ferritin, public health

Introduction

Acute infectious diseases continue to be a leading cause of morbidity and mortality in the paediatric population. Among these, the most common conditions include urinary tract infections (UTIs), acute respiratory tract infections (ARTIs), and gastroenteritis (GE). According to the World Health Organization (WHO), ARTIs account for approximately 18% of deaths and 8.2% of disabilities in children. UTIs affect approximately 4% of children under the age of five. (1)

Lower respiratory tract infections (LRTIs) involve inflammation of the airways below the larynx, extending to the lung parenchyma. (2) Common forms include bronchitis, bronchiolitis, and pneumonia. Nutritional deficiencies, particularly of iron, zinc, and vitamin A, compromise the immune system and increase susceptibility to infections such as LRTIs.(3)

A study by Behairy et al. demonstrated that 74% of ALRTI cases and 38% of controls had anaemia, with a statistically significant odds ratio of 4.64. Similarly, 60% of ALRTI cases had iron deficiency anaemia (IDA) compared to 24% in the control group, with an odds ratio of 4.75. (3)

Several socio-environmental factors also contribute to the risk of LRTIs, including low parental education, limited income, malnutrition, indoor air pollution, and lack of breastfeeding, as reported by Demissie et al.(4)

Anaemia, a widespread health issue primarily affecting pregnant women and young children, has a global prevalence of 47% in preschool children. It weakens the immune response and is associated with increased risk

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of LRTIs.(5) Iron plays a key role in oxygen transport, cellular respiration, immune function, and DNA synthesis. The connection between iron deficiency and LRTI is mediated by inflammatory cytokines such as TNF-α, IFN-γ, IL-1β, and IL-6, which are involved in immune dysregulation during infection.

Iron deficiency anaemia is most commonly seen in children between the ages of 8 months and 5 years. The prevalence is considerably higher in developing countries due to food insecurity, inadequate health education, and limited access to diagnostic and therapeutic services. Given the socioeconomic and clinical burden of LRTIs, it is crucial to explore preventable risk factors such as IDA that may contribute to disease development. The present study aims to examine the association between iron deficiency anaemia and lower respiratory tract infections in children, based on objective parameters including haemoglobin, mean corpuscular volume (MCV), serum ferritin, and serum iron levels, to facilitate early recognition and timely intervention.

Methodology

A case-control study was conducted over six months from January 2023 to June 2023 at the Department of Paediatrics, Pakistan Railway Hospital, Rawalpindi. A total of 70 children aged 1 to 5 years were enrolled using non-probability consecutive sampling. Participants were divided into two groups: 35 children presenting with signs and symptoms of lower respiratory tract infection (LRTI) were classified as cases, while 35 children attending for routine check-ups or without respiratory complaints served as controls.

Children with chronic systemic illnesses, congenital malformations, tuberculosis, diabetes mellitus, bronchial asthma, protein-energy malnutrition, or those currently receiving iron supplementation were excluded.

Sample size was calculated using the WHO sample size calculator, based on an expected prevalence of iron deficiency of 60% among cases and 24% among controls, with 90% power and a 5% level of significance.

Blood samples were collected under aseptic conditions by a trained phlebotomist using sterile disposable syringes. Samples were analysed for complete blood count (CBC), C-reactive protein (CRP), serum ferritin, and serum iron levels. Iron deficiency anaemia (IDA) was diagnosed based on the following criteria: haemoglobin <11 g/dL, mean corpuscular volume (MCV) <75 fL, serum ferritin <30 ng/mL, and serum iron <50 µg/dL.

LRTI was diagnosed in the presence of at least four of the following clinical features: fever >38.5°C, cough, tachypnoea (respiratory rate >40 breaths per minute), lower chest wall indrawing, sore throat, runny nose, or poor feeding. CRP levels greater than 6 mg/dL were considered elevated.

Demographic data and clinical findings were recorded using a structured data collection form. Data analysis was performed using SPSS version 27. Mean and standard deviation were calculated for continuous variables such as age, haemoglobin, MCV, serum iron, and ferritin. Categorical variables, including gender, socioeconomic status, and clinical symptoms, were expressed as frequencies and percentages.

The association between IDA and LRTI was evaluated using the chi-square test. A p-value ≤0.05 was considered statistically significant. Odds ratios (ORs) were calculated to quantify the strength of association. Effect modifiers, including age, gender, socioeconomic status, and residence, were controlled through stratification and post-stratification analysis using chi-square tests and ORs.

Results

A total of 70 children aged 1 to 5 years were enrolled in the study, including 35 cases diagnosed with lower respiratory tract infection (LRTI) and 35 controls without respiratory illness.

Among the cases, 20 (57.1%) were male and 15 (42.9%) were female. In the control group, 19 (54.3%) were male and 16 (45.7%) were female, with no significant difference in gender distribution between the groups ($p = 0.81$). The mean age of cases was 3.01 ± 1.09 years, while that of controls was 3.04 ± 1.02 years ($p = 0.899$).

Socioeconomic status (SES) differed significantly ($p = 0.036$), with a higher proportion of cases belonging to the lower SES category (62.9%) compared to controls (37.1%). Urban residence was predominant in both groups, with no statistically significant difference observed (cases: 68.6%, controls: 77.1%; $p = 0.40$).

Baseline demographic characteristics are summarised in **Table 1**.

Table 1. Demographic Characteristics of Study Participants

Variable	Cases (n=35)	Controls (n=35)	p-value
Mean Age (years)	3.01 ± 1.09	3.04 ± 1.02	0.899
Gender (Male)	20 (57.1%)	19 (54.3%)	0.81
SES – Lower	22 (62.9%)	13 (37.1%)	0.036*
Urban Residence	24 (68.6%)	27 (77.1%)	0.40

*Significant at p ≤ 0.05

Haematological Parameters

Significant differences were observed between cases and controls across all haematological parameters. Children with LRTI had a significantly lower mean haemoglobin level (9.23 ± 1.05 g/dL) compared to controls (11.58 ± 1.02 g/dL; p < 0.001). Mean corpuscular volume (MCV) was also significantly reduced in cases (68.51 ± 5.32 fL) compared to controls (76.29 ± 4.67 fL; p < 0.001).

Serum ferritin levels were lower among cases (21.37 ± 6.45 ng/mL) than controls (41.82 ± 8.51 ng/mL; p < 0.001), as were serum iron levels (36.62 ± 7.74 µg/dL in cases vs. 74.91 ± 9.23 µg/dL in controls; p < 0.001).

These findings are summarised in Table 2.

Table 2. Comparison of Haematological Parameters

Parameter	Cases (n=35)	Controls (n=35)	p-value
Haemoglobin (g/dL)	9.23 ± 1.05	11.58 ± 1.02	<0.001*
MCV (fL)	68.51 ± 5.32	76.29 ± 4.67	<0.001*
Serum Ferritin (ng/mL)	21.37 ± 6.45	41.82 ± 8.51	<0.001*
Serum Iron (µg/dL)	36.62 ± 7.74	74.91 ± 9.23	<0.001*

*Significant at p ≤ 0.05

Prevalence of Iron Deficiency Anaemia

Iron deficiency anaemia (IDA) was significantly more prevalent among children with LRTI, diagnosed in 21 (60.0%) of cases compared to 8 (22.9%) of controls (p = 0.002). The calculated odds ratio (OR) for IDA associated with LRTI was 5.04 (95% CI: 1.77–14.36), indicating that children with IDA were approximately five times more likely to develop LRTI than those without.

Table 3 summarises the association between IDA and LRTI.

Table 3. Association of Iron Deficiency Anaemia with LRTI

Group	IDA Present	IDA Absent	Total
Cases	21 (60.0%)	14 (40.0%)	35
Controls	8 (22.9%)	27 (77.1%)	35
Total	**29 (41.4%)**	**41 (58.6%)**	**70**

Chi-square = 9.78
p-value = 0.002*
Odds Ratio = 5.04 (95% CI: 1.77–14.36)

*Significant at p ≤ 0.05

Clinical Features of LRTI

Among children diagnosed with LRTI, the most common clinical features were:

Cough: 32 (91.4%)

Fever: 29 (82.9%)

Difficult breathing: 23 (65.7%)

Runny nose: 24 (68.6%)

Poor feeding: 20 (57.1%)

Lower chest wall indrawing: 19 (54.3%)

Sore throat: 15 (42.9%)

Elevated C-reactive protein (CRP) levels (>6 mg/dL) were observed in 28 (80.0%) of cases compared to only 4 (11.4%) of controls (p < 0.001).

Stratification Analysis

Stratified analysis showed that the association between IDA and LRTI remained statistically significant across different age groups and gender (p < 0.05). The association was particularly strong among children from lower socioeconomic backgrounds (p < 0.001). No significant effect modification was observed based on place of residence.

Discussion

This case-control study demonstrated a statistically significant association between iron deficiency anaemia (IDA) and lower respiratory tract infections (LRTIs) in children aged 1 to 5 years. IDA was diagnosed in 60% of LRTI cases compared to 22.9% of controls, corresponding to an odds ratio (OR) of 5.04 (95% CI: 1.77–14.36; p = 0.002). These findings indicate that children with IDA were approximately five times more likely to develop LRTIs than their non-anaemic peers, suggesting a strong and independent association between iron deficiency and increased infection risk.

The haematological profiles of affected children further support this association. Mean haemoglobin, serum ferritin, serum iron, and mean corpuscular volume (MCV) were significantly lower among cases than controls ($p < 0.001$ for all), confirming the presence of iron deficiency and anaemia in children presenting with LRTIs. These parameters align with established diagnostic criteria for IDA, strengthening the internal validity of the observed association. Moreover, a low haemoglobin level is recognised as a serious risk factor for the development of acute lower respiratory tract infections (ALRTIs). (6) Our findings are consistent with previous studies that have investigated the role of anaemia, particularly IDA, in predisposing children to respiratory infections. Behairy et al. reported a 60% prevalence of IDA in children with acute LRTIs and an OR of 4.75, closely mirroring our results. (3) Similarly, Osama Saleh et al. observed IDA in 55% of LRTI cases compared to 27.5% of controls, with a statistically significant association. (7) Stepan et al. further supported these findings by demonstrating a significant association between IDA and acute LRTIs in toddlers aged 1–3 years. (8) The consistency of these findings across diverse populations reinforces the conclusion that IDA is a significant and independent risk factor for LRTIs in early childhood.

The biological plausibility of this relationship is well established. Iron plays a vital role in both oxygen transport and immune function. Iron deficiency impairs cellular immunity by reducing the activity of neutrophils and macrophages, inhibiting cytokine responses such as interleukin-6 (IL-6), and altering the proliferation and differentiation of T-lymphocytes. (9) These immune impairments compromise the host's ability to contain and clear respiratory pathogens, thereby increasing susceptibility to infections such as pneumonia, bronchitis, and bronchiolitis. Furthermore, the relationship between IDA and the severity of respiratory disease (RD) may be explained by the role of iron in modulating immune responses and protecting against lung injury. Iron deficiency impairs cell-mediated immunity, suggesting that iron is directly involved in both the regulation of immune defence and the extent of pulmonary inflammation and damage. (10)

In our study, the association between IDA and LRTI persisted across age groups and genders. Notably, the relationship was more pronounced among children from lower socioeconomic backgrounds, consistent with findings by Demissie et al., who highlighted socioeconomic disadvantage as a key determinant of both anaemia and LRTIs.(4) This highlights the complex interplay between poverty, nutritional deficiencies, and infectious disease risk in early childhood. Public health initiatives aimed at improving maternal education(11), nutritional support programs, and early screening for IDA in underserved communities may play a pivotal role in reducing the burden of respiratory infections in young children.

Limitations

While the strength of the association is compelling, the single-centre design and relatively small sample size may limit generalizability.

Recommendations

Future multicenter studies are needed to further explore the potential benefits of routine iron supplementation in reducing the incidence and severity of LRTI.

Conclusion

This study provides compelling evidence of a strong and statistically significant association between iron deficiency anaemia (IDA) and lower respiratory tract infections (LRTIs) in children aged 1 to 5 years. Children with IDA were found to be five times more likely to develop LRTIs than non-anaemic peers, highlighting the critical role of iron in immune competence and respiratory health. The significant differences in haematological parameters between cases and controls further validate this link and highlight the utility of routine screening for iron deficiency in children presenting with respiratory symptoms.

Given the high burden of anaemia and infectious diseases in low- and middle-income settings, early identification and correction of iron deficiency may serve as an effective and accessible strategy to reduce the incidence and severity of LRTIs in early childhood. Addressing iron deficiency, especially among children from socioeconomically disadvantaged backgrounds, should be integrated into broader public health efforts aimed at improving child survival and wellbeing.

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