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Impact of Iron Deficiency Anemia on the Severity of Bronchiolitis in Pediatric Patients

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ABSTRACT

Bronchiolitis is an acute inflammatory respiratory illness involving the lower respiratory tract occurring in the first 2 years of life. **Objectives:** To determine the impact and outcomes of the severity of iron deficiency anemia (IDA) in patients with acute bronchiolitis (AB). **Methods:** This analytical, cross-sectional study was conducted in the Department of Pediatric Medicine, Ziauddin University Hospital, Karachi, Pakistan, from April 2025 to September 2025. A total of 126 children aged 2–23 months with AB were enrolled through non-probability consecutive sampling. Bronchiolitis severity was classified by the Wang score. Data were analyzed using SPSS version 26.0, with $p<0.050$ considered significant. **Results:** In 126 children, 73 (57.9%) were males, and the median age was 10.0 months (IQR 6.0–14.0). Mild IDA was present in 38 (31.2%), moderate in 64 (50.8%), and severe in 24 (19.0%) cases. With increasing anaemia severity, weight decreased (8.7 vs 7.6 kg; p=0.038), SpO_2 declined (92.4% vs 88.7%; p=0.016), respiratory rate rose (p=0.009), and Wang score increased (5.3 vs 9.4; p=0.004). Severe IDA showed longer tachypnoea resolution (5.1 vs 3.2 days; p<0.001), retraction recovery (6.2 vs 3.9 days; p=0.002), greater oxygen requirement (18 [75.0%] vs 13 [34.2%]; p=0.002), and prolonged hospital stay (7.2 vs 5.1 days; p<0.001). Severe IDA was significantly associated with severe bronchiolitis (p=0.004). **Conclusions:** The severity of IDA was strongly associated with worse clinical presentation and delayed recovery in children with acute bronchiolitis. Lower haemoglobin and microcytic indices correlated with higher Wang respiratory scores, greater oxygen support requirements, and longer hospital stays.

INTRODUCTION

Bronchiolitis is an acute inflammatory respiratory illness involving the lower respiratory tract occurring in the first 2 years of life [1]. Respiratory syncytial virus (RSV) is estimated to be involved in 60-80% of acute bronchiolitis (AB) cases among infants and may lead to severe disease and mortality in younger age groups [2, 3]. In Pakistan, AB affects around 5.7 per 10,000 population with approximately 2-3% of children requiring hospitalization within 1st year of life [4]. Gender, age, history of prematurity, and immunodeficiency or cardiopulmonary disease are some of the most commonly known risk factors for severe AB [5]. Although there is not enough evidence that significantly establishes the effect of iron deficiency anemia (IDA) on AB, IDA, by providing a hypoxic environment in the respiratory circulation, can be one of the major contributors to lower respiratory tract infections (LRTIs) among children below 5 years of age [6, 7]. A study revealed that, among patients with AB aged below 24 months, IDA was observed in 36.6% of them [8]. In a case-control study conducted by Roma *et al.* anemia was found in 72% of cases and 34% of controls, with 86% of the anemic patients in the study group and 63% in controls having iron deficiency [9]. Not much contemporary literature is on view explaining the relationship between IDA and AB among children below 2 years of age. The findings of this research were thought to provide important insights that may aid clinicians in better identifying and treating IDA in bronchiolitis patients, which may ultimately lessen the

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severity, length, and risk of complications of the illness. This study was planned with the aim of determining the impact and outcomes of the severity of IDA in patients with AB.

Although there is current evidence that iron deficiency anemia (IDA) is related to respiratory infections, there is a dearth of current data that specifically assesses its influence on the severity and clinical outcome of acute bronchiolitis in children under two years of age, especially in resource-limited areas where iron profile testing is not commonly performed. This leaves a loophole in knowledge about whether IDA has a solitary effect of deteriorating the disease and recovery. Thus, the gap that the current study will fill is the ambiguous role of the severity of IDA in determining the severity and outcomes of bronchiolitis. This study aims to establish the relationship between the severity of IDA and clinical severity, oxygen requirement, and outcome of recovery in children with acute bronchiolitis.

METHODS

This analytical, cross-sectional research was performed at the Department of Pediatrics, Ziauddin University Hospital, Karachi, Pakistan, from April 2025 to September 2025, after getting permission from the institutional ethical review committee (Ref. code: 9910225RAPED, dated: March 29, 2025). A sample size of 126 was calculated using the WHO sample size calculator by considering the anticipated frequency of IDA in children with AB as 80.0, with a 95% confidence level and a 7% margin of error [10]. The inclusion criteria were children of any gender, aged 2-23 months, diagnosed with acute bronchiolitis. The exclusion criteria were children with bronchopulmonary dysplasia, immunodeficiency, chronic lung disease (like cystic fibrosis), congenital or acquired heart disease, severe acute malnutrition, or neuromuscular disorders. All preterm children (≤34 weeks of gestation) or who left against medical advice (LAMA) within 24 hours of admission were also excluded. AB diagnosis was based on the presence of upper respiratory virus infection symptoms (like rhinorrhea, cough, and low-grade fever) and signs of lower respiratory tract involvement (like tachypnea, wheezing, crackles, or retractions) [11, 12]. A respiratory rate >50 breaths/min in children ≤ 1 year of age or a respiratory rate > 40 breaths/min in children > 1 year of age was considered tachypnea. The sampling technique used for sample selection was the "non-probability consecutive sampling technique". The parents/legal guardians were briefed about the objective and safety of the study before obtaining informed and written consent from them. At the time of admission, demographics, clinical, and vital information were noted. Using an aseptic technique, 5 mL of venous blood was drawn and sent to the institutional laboratory for a complete blood count (CBC) evaluation to mark IDA. Although IDA is diagnosed with iron profile studies, in the current resource-limited setting, where these tests might not be readily available for every patient, other CBC parameters, which included hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW), were used as the stand-in markers for IDA [13]. The parameters to label IDA included anemia (Hb level <11 g/dL), MCV <72 fL, RDW >14%, a mean corpuscular hemoglobin (MCH) <27 pg/cell, and a Mentzer index (MCV/RDW) >13 [13, 14]. Wang bronchiolitis severity scores (WBSS) classified bronchiolitis as mild (1-3), moderate (4-8), or severe (9-12) bronchiolitis, using the clinical factors, which included respiratory rate, wheezing, retractions, and general appearance [15]. Severity scoring was done by the researchers themselves at the time of admission and then subsequently every 24 hours until discharge. All the patients were offered standard recommended care for bronchiolitis, including oxygen support, nebulization with hypertonic saline, hydration support, and frequent suction of nasal and oral secretions. The need for noninvasive ventilation (yes/no), duration of oxygen requirement (days), PICU stay (days), and hospital stay (days) were noted at the time of discharge. Discharge criteria were followed as per the hospital protocol for bronchiolitis. The association of IDA with the severity of bronchiolitis and its outcomes (duration of resolution of tachypnea, duration of resolution of retraction, and duration of hospital stay) was assessed. IDA was categorized as mild (Hb 10.0-10.9 g/dl), moderate (7.0-9.9 g/dl), and severe (Hb<7.0 g/dl) [16]. All of the relevant information was collected on a structured proforma, especially designed for this study.

The statistical analysis was performed using "IBM-SPSS Statistics" version 26.0. The qualitative variables were shown as frequency and percentage. The normality of the quantitative data was tested using the Shapiro-Wilk test. For the representation of numeric variables, means and standard deviations (SD) or medians and interquartile ranges (IQR) were computed, depending upon the normal distribution of the data. Effect modifiers were controlled by making a stratified table, and post-stratification, chi-square test, or analysis of variance / Kruskal-Wallis' test were applied with respect to IDA severity, taking $p<0.050$ as significant.

RESULTS

In a total of 126 children, the median age was 10.0 months (IQR 6.0–14.0). There were 73 (57.9%) males and 53 (42.1%) females. The overall median Hb was 9.2 g/dL (IQR 8.3–10.1), with corresponding red cell indices showing a microcytic, hypochromic pattern. The median MCV was 68.0 fL (IQR 63.5–72.0), mean MCH 25.0 pg (IQR 22.8–26.9), and red cell

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distribution width (RDW) 15.3% (IQR 14.5–16.4). The Mentzer index was 12.6 (IQR 11.8–13.3), consistent with IDA. At the time of admission, the median oxygen saturation (SpO_2) was 91.0% (IQR 88.0–94.0). The median respiratory rate was 52 breaths/min (IQR 46–60), and the heart rate was 138 beats/min (IQR 124–148). Among these 126 children, 38 (31.2%) had mild IDA, 64 (50.8%) moderate IDA, and 24 (19.0%) severe IDA. Significant declining trend in age was seen with respect to the severity of IDA (p=0.041). The median weight progressively declined with increasing anemia severity (p=0.038). Oxygen saturation at admission showed a significant downward trend across anemia categories (p=0.016). The respiratory rate increased progressively with respect to the severity of IDA (p=0.009). The median Wang respiratory score increased from 5.3 (IQR 3.1–6.9) in mild IDA to 9.4 (IQR 7.4–10.9) in severe IDA (p = 0.004), indicating greater bronchiolitis severity with worsening anemia. The median Hb decreased from 10.5 g/dL (IQR 10.2–10.8) in mild IDA to 6.5 g/dL (IQR 6.2–6.8) in severe IDA (p<0.001). The median MCV (p<0.001), and median MCH (p=0.002) declined significantly with increasing anemia severity. The RDW increased significantly with respect to the severity of IDA (p=0.004) (Table 1).

Table 1: Comparison of Baseline Characteristics of Children with Bronchiolitis According to Severity of Iron Deficiency Anemia (n=126)

Characteristics	Severity of Iron Deficiency Anaemia			p-value
	Mild (n=38)	Moderate (n=64)	Severe (n=24)	
Male	20 (52.6%)	39 (60.9%)	14 (58.3%)	0.870*
Female	18 (47.4%)	25 (39.1%)	10 (41.7%)	
Age (months)	12.0 (8.5-15.2)	9.5 (6.0-13.0)	8.4 (5.8-10.1)	0.041^
Weight (kg)	8.7 (7.9-9.6)	8.2 (7.3-9.0)	7.6 (7.0-8.5)	0.038^
SpO2 at Admission (%)	92.4 (90.3-94.8)	91.1 (88.2-93.5)	88.7 (86.1-90.8)	0.016^
Respiratory Rate (breaths/min)	48.7 (44.5-53.6)	53.2 (48.1-60.5)	56.8 (50.3-63.9)	0.009^
Heart Rate (beats/min)	132.5 (12.4-143.6)	138.6 (126.2-149.3)	142.9 (133.4-155.8)	0.073^
Wang Respiratory Score	5.3 (3.1-6.9)	7.1 (5.2-9.3)	9.4 (7.4-10.9)	0.004^
Haemoglobin (g/dl)	10.5 (10.2-10.8)	8.7 (8.2-9.3)	6.5 (6.2-6.8)	<0.001
Mean Corpuscular Volume (fL)	72.1 (69.5-74.0)	67.2 (63.1-70.3)	62.6 (60.1-65.2)	<0.001^
Mean Corpuscular Haemoglobin (pg)	26.6 (25.0-28.1)	24.8 (22.7-26.4)	22.5 (21.0-23.9)	0.002^
Red cell distribution width (%)	14.3 (13.7-15.1)	15.5 (14.8-16.3)	16.4 (15.5-17.3)	0.004^

^ Kruskal–Wallis Test Applied; Values Are Median (IQR); * Chi-Square Test Applied

Bronchiolitis severity, assessed by Wang scoring, was significantly associated with severity of IDA (p=0.004). Among children with mild IDA, 17 (44.7%) had mild bronchiolitis, 14 (42.1%) had moderate, and 5 (13.2%) had severe bronchiolitis. In contrast, among those with severe IDA, 3 (12.5%) had mild, 9 (37.5%) had moderate, and 12 (50.0%) had severe bronchiolitis. Odds ratio for severe bronchiolitis in severe versus mild IDA was 6.6 (95% CI: 2.0–21.4), indicating a markedly higher likelihood of severe bronchiolitis in children with severe IDA compared with mild IDA (Table 2).

Table 2: Association Between Severity of Iron Deficiency Anemia and Severity of Bronchiolitis (n=126)

Bronchiolitis Severity	Severity of Iron Deficiency Anaemia			p-value
	Mild (n=38)	Moderate (n=64)	Severe (n=24)	
Mild (Wang 1-3)	17 (44.7%)	16 (25.0%)	3 (12.5%)	0.004
Moderate (Wang 4-8)	16 (42.1%)	33 (51.6%)	9 (37.5%)	
Severe (Wang 9-12)	5 (13.2%)	15 (23.4%)	12 (50.0%)	

Chi-square applied

The duration required for resolution of tachypnea increased from 3.2 days (IQR 2.4–4.1) in mild IDA to 5.1 days (IQR 4.0–6.2) in severe IDA (p<0.001). Retraction resolution prolonged from 3.9 days (IQR 3.0–5.1) to 6.2 days (IQR 5.1–7.9) (p=0.002). Oxygen support was required in 13 (34.2%) children with mild, 33 (51.6%) with moderate, and 18 (75.0%) with severe IDA (p=0.002). Although PICU admission increased from 3 (7.9%) in mild to 7 (29.2%) in severe IDA, the difference was not statistically significant (p=0.109). The duration of hospital stays increased from 5.1 days (IQR 4.3–6.2) in mild anemia to 7.2 days (IQR 6.0–9.0) in severe anemia (p<0.001). Details about clinical outcomes with respect to anemia severity are given (Table 3).

Table 3: Comparison of Clinical Outcomes According to the Severity of Iron Deficiency Anemia

Outcomes	Severity of Iron Deficiency Anaemia			p-value	Differences Between Severe vs. Mild IDA
	Mild (n=38)	Moderate (n=64)	Severe (n=24)		
Tachypnea-Resolution (Days)	3.2 (2.4-4.1)	4.0 (3.2-5.2)	5.1 (4.0-6.2)	<0.001^	1.9 days (95% CI: 1.1-2.5)
Retraction-Resolution (Days)	3.9 (3.0-5.1)	5.0 (4.1-6.3)	6.2 (5.1-7.9)	0.002^	2.3 days (95% CI: 1.2-3.1)
Oxygen Support	13 (34.2%)	33 (51.6%)	18 (75.0%)	0.002*	40.8% (95% CI: 17.8%-63.8%)
PICU Admission	3 (7.9%)	7 (10.9%)	7 (29.2%)	0.109*	21.1% (1.2%-41.4%)

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Hospital Stays (Days)	5.1 (4.3-6.2)	6.0 (5.0-7.3)	7.2 (6.0-9.0)	<0.001^	2.1 days (95% CI: 1.4-2.8)

^Kruskal–Wallis test; *Chi-square test; quantitative data = median (IQR)

DISCUSSION

This study found a significant association between Hb concentration and bronchiolitis severity, as children with severe IDA had a median Hb of 6.5 g/dL compared with 10.5 g/dL in mild IDA. This aligns with the results of Celik *et al.* who reported that bronchiolitis cases with Hb ≤10 g/dL were 10 times more likely to develop severe disease, with a negative correlation between Hb and severity (r=-0.423, p<0.001) [5]. These findings may highlight a potentially important role of IDA in aggravating hypoxemia and inflammatory responses during LRTIs [17]. The association of IDA with higher Wang scores in the present analysis is consistent with Gupta *et al.* who documented IDA in 70% of bronchiolitis cases compared with 35% of controls (p=0.001) [10]. That study showed significant differences in MCV, MCH, and transferrin saturation between affected and control groups. The parallel findings reinforce that microcytosis and hypochromia represent the hematologic background favoring poorer respiratory outcomes. In the current study, significant deterioration in oxygen saturation and an increase in respiratory rate were observed with worsening anemia. Ragab *et al.* also demonstrated that infants with moderate and severe bronchiolitis had significantly lower Hb. and MCHC, with reduced serum iron and elevated TIBC in the severe group [18]. They identified Hb and serum iron as independent predictors of bronchiolitis severity, supporting the physiological plausibility that reduced oxygen-carrying capacity exacerbates hypoxemia and increases respiratory workload [18]. In the present work, the duration of hospital stays progressively increased with anemia severity. Sahu *et al.* similarly found that lower MCV, MCH, and serum iron levels in AB cases were correlated with prolonged hospitalization [19]. A study from Sri Lanka described the frequency of anemia to be significantly higher among children with acute LRTIs than controls (odds ratio: 1.6, p=0.045). Oxygen support was needed in 75% of children with severe IDA in this study compared with 34% with mild IDA. There may be a role of IDA in impairing tissue oxygenation and respiratory muscle endurance, resulting in increased dependency on supplemental oxygen, but these assumptions require further research [20]. In this study, the severity of AB inversely correlated with Hb and directly with RDW, which may indicate greater erythrocyte size variability in severe anemia. Reported that RDW proportion was significantly higher among bronchiolitis patients compared to controls (p<0.050) [21]. Multiple other studies have observed that anemia, particularly IDA, clearly increases the susceptibility to and severity of LRTIs [9, 22]. The biological mechanism linking iron deficiency to severe bronchiolitis lies in impaired oxygen transport and altered immune defense [23]. Iron plays a pivotal role in cellular respiration, epithelial repair, and cytokine regulation. Deficiency results in decreased tissue oxygenation, diminished oxidative burst capacity of neutrophils, and impaired mucosal immunity [21, 24]. These physiological effects may collectively increase viral replication and inflammatory injury in bronchioles, leading to more severe clinical manifestations [25].

Single-centre study design with relatively modest sample size reduces the generalizability of these findings. The cross-sectional design restricted the ability to infer temporal causation between anemia and bronchiolitis severity. IDA diagnosis was based on hematological indices because iron profile testing, such as serum iron, ferritin, and transferrin saturation were not consistently feasible due to resource limitations. Longitudinal follow-up could clarify whether correction of anemia leads to improved clinical outcomes. It is suggested to conduct longitudinal and multicenter studies in the future to establish causal relationships and enhance generalizability. To improve the diagnostic accuracy, the complete iron profile parameters (e.g., serum ferritin, transferrin saturation) should be incorporated. Moreover, interventional research to evaluate the impact of early iron correction on bronchiolitis results is justified.

CONCLUSIONS

The severity of IDA was strongly associated with worse clinical presentation and delayed recovery in children with acute bronchiolitis. Lower Hb and microcytic indices correlated with higher Wang respiratory scores, greater oxygen support requirements, and longer hospital stays.

Authors' Contribution

Conceptualization: FZ
Methodology: RA
Formal analysis: RA
Writing and Drafting: RA, FZ, RM
Review and Editing: RA, FZ, RM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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