

A Study to Evaluate Whether Iron Deficiency Anemia is Associated with Acute BronchiolitisAbu Irfan¹, Baibhav Prakash Sahay², S. Bhushan³¹Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India²Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India³Professor and HOD, Department of Pediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India

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Conflict of interest: Nil

Abstract**Aim:** The aim of the present study was to evaluate whether iron deficiency anemia is associated with acute bronchiolitis**Material & Methods:** This Cross-Sectional Analytical study was carried out in the Department of Paediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for the period of 24 months after obtaining ethical approval to explore the association between iron deficiency anemia and bronchiolitis. For this purpose, a total number of 200 patients were enrolled in the study and among them, 100 children with bronchiolitis were considered as cases, and 100 healthy children without bronchiolitis were considered as control, who were matched with age.**Results:** Majority of the patients were in the age group between 13-18 months. The mean age was found 13.087±5.735 months in cases and 15.125±7.963 months in controls. The mean age difference was not significant between the two groups ($p>0.05$). Male participants (65%) were the predominant group in the study and female participants (35%). Exclusive breastfeeding was found in 39 cases and 64 controls respectively. The differences were statistically significant ($p<0.05$) between the two groups in the chi-square test. Overcrowding was found in 76 cases and 60 controls respectively. There was a significant difference in Hb (gm/dl) between cases and controls followed by MCV (fl) between cases and controls. The MCH (pg) level was statistically and significantly lower in cases compared to controls; followed by MCHC (g/dl) which was statistically and significantly lower in cases compared to controls. S. Iron ($\mu\text{g/dl}$) was statistically and significantly lower in cases compared to controls. Transferrin Saturation (%) was statistically and significantly lower in cases compared to controls. RDW-CV (%) was statistically and significantly higher in cases compared to controls. Among the 200 study subjects 80 cases had anemia, followed by 60 controls had anemia. Their difference was statistically significant between the two groups ($p<0.05$).**Conclusion:** Iron deficiency anemia has a significant association with bronchiolitis. A larger and more extensive study was recommended.**Keywords:** Iron deficiency anemia, Acute bronchiolitis, Children.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Iron Deficiency Anaemia (IDA) is one of the most common nutritional deficiencies worldwide. [1] The World Health Organization (WHO) estimates that the IDA burden is more than 2 billion worldwide. [2] Various studies have reported that IDA in children of the developing world varied from 0.5-15%. [3,4] However, in underdeveloped countries, the situation is alarming. As per an estimate reported in an Indian study, IDA prevalence in children is 69.5%. [5] It is stated that children under one year

of age are at higher risk of developing IDA due to the increased requirement of iron during growth and pregnancy. [6,7]

Iron is an essential component to maintain proper immune function, but the relationship with the disease conditions is complex. [8] Iron plays a vital role in both innate and adaptive immunity. Intracellular iron promotes the release of reactive oxygen species via activation of NF- κ B (Nuclear factor kappa B). The iron-dependent transcription factor and hypoxia-inducible factor-1 α promote

macrophages for the production of antimicrobial peptides. Administration of iron to iron-deficient patients has been shown to increase tumor necrosis factor α (TNF- α), interleukin 10 (IL-10), and IL-6 mRNA expression in peripheral blood mononuclear cells. Some animal studies have shown that reduced iron levels for various reasons have shown low levels of mature B cells and impaired T-cell development. [9] Acute infections are common among children and are associated with high morbidity and mortality. Acute respiratory tract infections (ARTIs), urinary tract infections (UTIs), and gastroenteritis (GE) are common infectious entities in children. [10]

Blood hemoglobin concentration is affected by different factors such as age, sex, altitude, ethnicity, active and passive smoking, and pregnancy. Therefore, these factors should be taken into the consideration and need to be adjusted before diagnosing anemia in a child. [11] There are some risk factors for bronchiolitis like non breast feed baby, living in crowded conditions, passive smoking, wood burning stoves, prematurity, low birth weight etc. [12] Anemia is identified as a risk factor for lower respiratory tract infection. [13] Anemia is one of the most common nutritional problems in the world and is associated with increased risk for morbidity and mortality especially, among under the 5 years of age and iron deficiency is considered the most common cause of anemia in developing countries. [14] In developing nations, IDA exceeds 50% and inadequate nutrition is typically blamed for it. [15,16] As anemia and bronchiolitis is common in our country, so this study was carried out to find the association between anemia and bronchiolitis.

Material & Methods

This Cross-Sectional Analytical study was carried out in the Department of Paediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for the period of 24 months after obtaining ethical approval to explore the association between iron deficiency anemia and bronchiolitis. For this purpose, a total number of 200 patients were enrolled in the study and among them, 100 children with bronchiolitis were considered as cases, and 100 healthy children without bronchiolitis were considered as control, who were matched with age.

Inclusion Criteria

- Children from 1 month to 2 years of age attended in the Department of Paediatrics with clinical and radiological findings of bronchiolitis were included.

Exclusion Criteria

- Patients with Chronic respiratory disease.
- Congenital heart disease.

- Consolidation or atelectasis on a chest roentgenogram.
- Severe systemic illness (e.g., malnutrition, tuberculosis) were excluded.

Study Procedure

The study cases were selected from IPD who were from 1 month to 24 months old with a history of runny nose, cough, breathing difficulty, chest indrawing and rhonchi on auscultation. Age-matched control was selected from outdoor healthy children without ALRTI. Informed written consent were taken from the mother or father or any legal attendant of the child. Information was collected by interviewing, from clinical and laboratory findings. Data was collected in a structured questionnaire. Both study case and control were investigated for Hb, RBC count, RBC Indices, PBF, Serum Iron, TIBC, and Transferrin Saturation. Transferrin Saturation was calculated using the formula of Iron level/TIBC. The cutoff point for low hemoglobin level is 11 gm/dl as per WHO definition. Blood samples were taken from the antecubital vein of each child by phlebotomist. Sterile, disposable syringes and needles, and proper tubes were used. Each sample was divided into 2 parts: one part (2 ml) put into a K3EDTA tube for CBC and the other part (3 ml) put into plain vacutainers for serum iron and TIBC. Serum was obtained at 3000/RPM for 5 minutes by lab rotator. Serum ferritin level was not investigated as in cases with infection, it increases probably as acute phase protein.

Laboratory Analysis

Hb% and RBC indices were analyzed by fully Automated Pentra DX Nexus (Horiba Medical) Haematology Analyzer, Japan, and verified manually by Hematologist. S. iron and TIBC were determined by using Chemiluminescent Microparticle Immune Assay (CMIA/ELIZA) by Mindray BS-230, Automated Biochemical Analyzer, China. Transferrin Saturation (%) is calculated by using the formula

$$\text{Transferrin Saturation} = (S. \text{Iron} \div S. \text{TIBC}) \times 100.$$

Statistical Methods

The numerical data obtained from the study, was analyzed, and the significance of differences was estimated by using statistical methods. Computer-based Statistical Package for Social Science (SPSS) version 23 was used. Qualitative values were expressed as frequencies and percentages and numerical data were expressed as Mean \pm SD. The comparison between the groups was done for the qualitative variables using a Chisquare test. When the conditions for Chi-square validity were not met, it was replaced by Fisher's exact test. The association between pathology (bronchiolitis) and potential causal factors (IDA) was described by the

relative risk and its confidence intervals. Continuous variables were compared through Student's t-test. P-value of 0.05 or less was considered significant.

Results

Table 1: Distribution of study subjects according to age in months

Age (months)	Case (N=100)	Control (N=100)	P value
1-6	40	20	
7-12	20	26	
13-18	24	26	0.316
19-24	16	28	
Mean±SD	13.087±5.735	15.125±7.963	

Majority of the patients were in the age group between 13-18 months. The mean age was found 13.087±5.735 months in cases and 15.125±7.963 months in controls. The mean age difference was not significant between the two groups ($p>0.05$).

Table 2: Gender distribution

Gender	N	%
Male	65	65
Female	35	35
Total	100	100

Male participants (65%) were the predominant group in the study and female participants (35%).

Table 3: Distribution of study subjects according to the risk factors

Risk Factors	N	%	P value
Exclusive breastfeeding			
Present	30	64	0.001
Absent	70	36	
Overcrowding			
Yes	76	60	0.088
No	24	40	
Cooking			
Gas	72	84	0.315
Wood	28	16	
Smoking in family			
Present	70	68	0.889
Absent	30	32	
Family history of atopy			
Present	8	16	0.412
Absent	92	84	

Exclusive breastfeeding was found in 39 cases and 64 controls respectively. The differences were statistically significant ($p<0.05$) between the two groups in the chi-square test. Overcrowding was found in 76 cases and 60 controls respectively.

Table 4: Comparison of lab findings in between case and controls

Investigation findings	Case	Control	P value
	Mean±SD	Mean±SD	
Hb (gm/dl)	9.51±1.66	10.64±2.15	0.007
TWBC (cmm)	16032.34±23312.14	8886.34±2034.06	0.084
MCV (fl)	73.27±10.72	75.85±7.93	0.048
MCH (pg)	23.57±4.56	24.48±3.47	0.038
MCHC (g/dl)	31.62±1.66	32.67±1.78	0.018
S.Iron(µg/dl)	42.08±21.35	64.36±22.54	<0.001
TIBC (µg/dl)	386.84±74.16	352.94±72.08	0.089
Transferrin Saturation (%)	12.44±8.42	17.83±9.02	0.005
RDW-CV (%)	15.34±2.76	14.16±1.96	0.052
Mentzer Index	17.43±4.16	16.33±2.38	0.190

There was a significant difference in Hb (gm/dl) between cases and controls followed by MCV (fl) between cases and controls. The MCH (pg) level

was statistically and significantly lower in cases compared to controls; followed by MCHC (g/dl) which was statistically and significantly lower in

cases compared to controls. S. Iron ($\mu\text{g}/\text{dl}$) was statistically and significantly lower in cases compared to controls. Transferrin Saturation (%) was statistically and significantly lower in cases

compared to controls. RDW-CV (%) was statistically and significantly higher in cases compared to controls.

Table 5: Association of anemia and IDA with acute bronchiolitis in study population

	Case (N=100)	Control (N=100)	p-value
Anemia			0.007
Anemic	80	60	
Non-anemic	20	40	
IDA			0.001
Present	60	30	
Absent	40	70	

Among the 200 study subjects 80 cases had anemia, followed by 60 controls had anemia. Their difference was statistically significant between the two groups ($p < 0.05$).

Discussion

A person can be considered anemic when the blood haemoglobin concentration is below 2 standard deviations below the mean for age. [17] Ineffective erythropoiesis, hemolysis, and blood loss are the main mechanisms responsible for the development of anemia. The most common contributing factors for anemia are nutritional deficiencies, disease, and genetic haemoglobin disorders. The three most common causes of anemia worldwide are iron deficiency, hemoglobinopathies, and malaria. Around 80% of hemoglobinopathies occur in low- and middle-income countries. Sick cell disorder is the most common hemoglobinopathy, and it is predominant in sub-Saharan Africa. The next in line is β - and α -thalassemia, predominant in South-East Asia. [18]

Majority of the patients were in the age group between 13-18 months. The mean age was found 13.087 ± 5.735 months in cases and 15.125 ± 7.963 months in controls. The mean age difference was not significant between the two groups ($p > 0.05$). Male participants (65%) were the predominant group in the study and female participants (35%). Kumar et al observed a male predominance in their study and male to female ratio was 1.3:1, which indicates male children are more prone to ALRI as compared to female children. [19] Exclusive breastfeeding was found in 39 cases and 64 controls respectively. The differences were statistically significant ($p < 0.05$) between the two groups in the chi-square test. Overcrowding was found in 76 cases and 60 controls respectively. The differences were statistically significant ($p < 0.05$) between the two groups found that non-breast-fed children had a 3.6-fold risk of ALRTI. [20]

Robledo-Aceves M et al [21] observed no significant ($p > 0.05$) association with smoking history in the family showed that only exposure to cigarette smoking was an independent risk factor

associated with severe bronchiolitis (OR, 3.5; 95% CI, 1.99-6.18; $p = 0.0001$). There was a significant difference in Hb (gm/dl) between cases and controls followed by MCV (fl) between cases and controls. The MCH (pg) level was statistically and significantly lower in cases compared to controls; followed by MCHC (g/dl) which was statistically and significantly lower in cases compared to controls. S. Iron ($\mu\text{g}/\text{dl}$) was statistically and significantly lower in cases compared to controls. Transferrin Saturation (%) was statistically and significantly lower in cases compared to controls. RDW-CV (%) was statistically and significantly higher in cases compared to controls. Among the 200 study subjects 80 cases had anemia, followed by 60 controls had anemia. Their difference was statistically significant between the two groups ($p < 0.05$). Behair et al [22] stated that there was a statistically significant increased incidence of anemia in group I compared with group II, with OR of 4.64 and 95% CI: (1.99-10.80). In their study, it was shown that 74 (74%) of 100 cases and 38 (38%) of 100 controls were anemic and 60 (60%) of cases and 24 (24%) of controls had IDA, with OR of 4.75 and 95% CI: 2.02-11.14 found a statistically higher percentage of IDA among cases (55%) than among controls (27.5%) ($p = 0.03$) stated a total of 82 cases with ALRTI, 34 cases were IDA positive fulfilling all six criteria, remaining was labelled as IDA negative showed that among the anemic children, 62 (86%) in the study group had iron deficiency.

Conclusion

The study has shown that iron deficiency anemia is associated with acute bronchiolitis in children from 1 month to 2 years of age. Moreover, children with iron deficiency anemia are 5 times more susceptible to acute bronchiolitis as compared to healthy control.

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