

Is Low Hemoglobin Level a Risk Factor for Acute Lower Respiratory Tract Infections?

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Abstract

Objective: This prospective study was conducted to evaluate whether a low hemoglobin level, was a risk factor for Acute Lower Respiratory Tract Infections (ALRTI) in children. **Methods:** 150 Children of all age groups who came to the outpatient department and those admitted for ALRTI were included in the study. Age and sex-matched 140 children, not having any respiratory illness, were taken as control. The study period was from March 2006 - March 2007. Detailed clinical and laboratory evaluation of the enlisted patients was done. All were subjected to detail investigations. **Results:** Radiological evidence of pneumonia was present in 70 (50 %) children. Hyperinflated lungs were seen in 40 (29%) and was normal in 30 (21.4%) cases. Blood culture was positive in 14 (10%) children of study group and none among control group. Klebsiella was the commonest organism isolated 6 (4.2%) in blood culture positive cases. The mean Hemoglobin (Hb) level of study group was 9.88 gm% and it was 12 gm% in control group. 96 (68.6%) of study group and 30 (21.42%) of control group had anemia. Of the anemic children, 79 (82.3%) in study group had iron deficiency, and 17 (17.7%) had normocytic normochromic anemia. These values were 18 (33.3%) and 36 (66.6%) respectively for control group. Low hemoglobin level was a risk factor ($p < 0.001$) ALRTI. **Conclusion:** Anemic children were 3.2 times more susceptible to ALRTI compared to the control group and iron deficiency anemia was predominating. Supplemental iron therapy may reduce the incidence of ALRTI. Prevention of anemia, due to whatever etiology is also essential.

Key words: ALRTI, anemia, hemoglobin.

Introduction

Anemia is a major nutritional global problem of immense public health significance, affecting persons of all ages, sex and economic group. It is ranked as the commonest chronic malady of mankind affecting approximately 30% i.e. 1500 million people all over the world. Iron deficiency anemia in children occurs most frequently between the age of 6 months to 3 years¹, the age when repeated infection occurs. On an average, children below 5 years of age suffer about 5-6 episodes of ALRTI per year². With this view the present study was conducted to see if children with iron deficiency anemia were at higher risk of ALRTI.

Methods

This prospective study was carried out for a period of one year from March 2006 – March 2007 in pediatric department of Manipal Teaching Hospital, Pokhara. A total of 290 (150 cases and 140 controls) children from 1 month to 5 years of age attending outpatient department and those hospitalized were studied. Controls were age and sex matched children not having respiratory problems. The inclusion criteria for cases were children with fever, cough, and fast respiratory rate, chest indrawing as per WHO criteria, and ronchi or crepitations on auscultation. The exclusion criteria was children suffering from other systemic illnesses like

Congenital heart disease, tuberculosis (any evidence plus Montaux test positive cases) and Protein Energy Malnutrition (PEM > Grade III as per Indian Academy of Pediatrics (IAP) classification). Children who already received antibiotic from outside were also excluded from the study. The purpose of the study was explained to the parents or guardians. Then consent was taken from parents or guardians before they were subjected to investigations. The investigations in both case and control included; complete blood count (CBC) with a peripheral smear, blood culture and sensitivity test, and X-ray chest, serum iron and serum iron binding capacity. Serum ferritin level was not done. Cyanmeth method by colorimeter was used to identify Hb level. Hemoglobin level < 10 gm % will be considered low in this study. Data were analysed using SPSS 10.0 by logistic multinomial regression analysis.

Results

Out of 290 children 150 were cases among which 10 were Mantoux positive hence was excluded from the study. Therefore the final figure was 140 (99 males and 41 females) cases and 140 (94 males and 46 females) controls. Among the cases 10 (8 males and 2 females) were less than 2 months, 69 (43 M and 26 F) were inbetween 2months – 1 year and 61 (48M and 13F) were above 1 year. Similarly for control group the distribution was 10 (6M/4F), 50(30M/20F), and 80 (58M/22F) were ≤2months, 2mo-1year and >1 year respectively. (Table1). Fever, cough and shortness of breath was main clinical features in the cases whereas fever, pain abdomen diarrhea, vomiting, seizures was

main clinical features in the control group (Table 2). Radiological evidence of pneumonia was present in 70 (50 %) children, hyperinflated lungs in 40 (29%) cases and normal in 30 (21.4%) cases (Fig 1). Out of 40 children who had hyperinflated lung fields 20 (50%) had a history of recurrent wheeze (fig.2) and 10 (25%) gave a positive family history of asthma. Blood culture was positive in 14 (10 %) children of study group (Table 3) and none among control group. Among the culture positives klebsiella was isolated in 6 (4.2%), and growth of staphylococcus, streptococcus pneumoniae, acintobacter and E.coli was noted in 2 (1.43%) cases each. The mean Hb level of study group was 9.88 gm% and it was 12 gm% in control group.96 (68.6%) of study group and 30 (21.42%) of control group had anemia. Of the anemic children, 79(82.3%) in study group had iron deficiency, with mean MCV 64 (fl),Mean MCH 17pg,MCHC 25gm/dl,Mean S. Iron 35µg/dL,Mean TIBC 390µg/dL.17 (17.7%) had normocytic normochromic anemia. These values were 18 (33.3%) [With mean MCV 68.7 (fl), Mean MCH 15pg, Mean MCHC 27gm/dl, Mean S. Iron 35µg/dL, Mean TIBC 350µg/dL] and 36 (66.6%) respectively for control group (Table 4). There were 72 cases of bronchopneumonia among which 62 (86%) of them were anemic whereas rest 68 were wheeze associated ALRTI (bronchiolitis & recurrent wheeze) of which 34 (50%) were anemic.(Table 5). Descriptive data regarding multivariate logistic regression analysis showing the risk factor of ALRTI. Table 7 reveals the montaux positive cases which were excluded from the study.

Table 1: Age and Sex distribution of cases and control

Sex	Age			Total
	≤2 months	>2mo-1yr	>1 -5 year	
Case ; Male=99 (70.7%) Female=41(29.3%)	8 2	43 26	48 13	140
Total	10	69	61	140
Control: Male= 94 (67%) Female=46 (32.8%)	6 4	30 20	58 22	140
Total	10	50	80	140

Table 2: Symptoms and signs at presentation

Symptoms	Case		Control	
	N (n=140)	Percentage	N(n=140)	Percentage
Fever	135	96.42%	114	81.42%
Cough	140	100%	8	5.71%
Shortness of breath	81	57.85%	4	2.85%
Convulsion	10	7.14%	30	21.42%
Vomiting	29	20.71%	77	55%
Diarrhea	10	7.14%	52	37.14%
Noisy breathing	50	35.71%	0	0%
Poor feeding	80	57.14%	60	42.85%
Chest pain	4	2.85%	0	0%
Irritable	20	14.28%	30	21.42%
Fast breathing	100	71.42%	0	0%
Delayed development	0	0%	6	4.28%
Headache	0	0%	2	1.42%
Pain abdomen	0	0%	35	25%
Sore throat	0	0 %	24	17%
Signs				
Chest indrawings	120	85.71%	0	0%
Ronchi	70	50%	0	0%
Crepitations	60	42.85%	0	0%
Pyoderma	0	0%	4	2.85%
Dehydration	5	3.57%	35	25%

Table 3: Blood culture of cases and control

Blood culture	Case (n=140)		Control (n=140)	
	Number	Percentage	Number	Percentage
No growth	126	90 %	140	100%
Growth	14	10%	0	0%
<i>Klebsiella</i>	6	4.2%		
<i>Staphylococcus</i>	2	1.43%		
<i>S. Pneumniae</i>	2	1.43%		
<i>Acintobacter</i>	2	1.43%		
<i>E.coli</i>	2	1.43%		

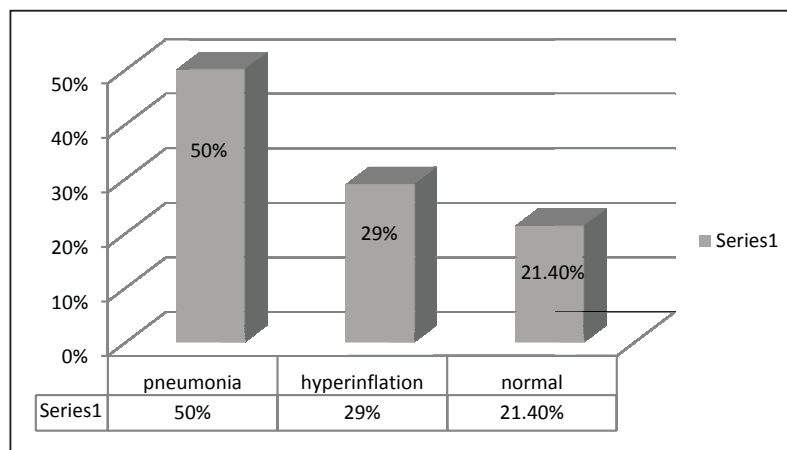


Fig. 1: Radiological findings of cases

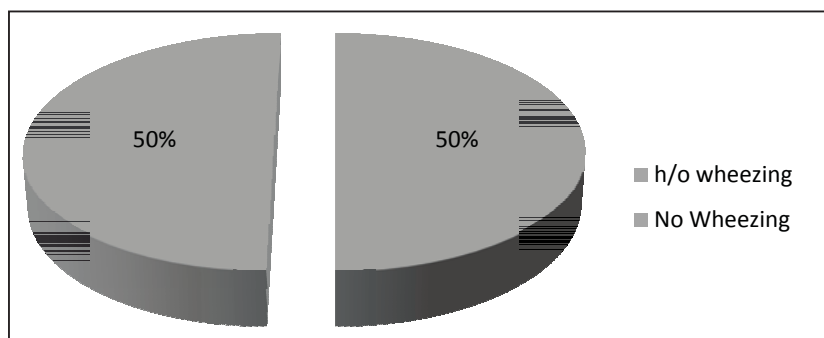


Fig. 2: History of wheezing

Table 4: Hemogram of Cases and Control.

	Case (n=140)		Control (n=140)	
	Number	Percentage	Number	Percentage
Mean Hb	9.88gm %		12gm %	
Hemoglobin				
≤10gm%±	96	68.6%)	54	38.6%
>10gm%	44	31.4%	86	61.4%
Anemia type				
MH*	79	82.3%	18	33.3%
NN**	17	17.7%	36	66.6%
	MH anemia	NN anemia	MH anemia	NN anemia
Mean MCV(fl)***	64	80	68.7	79
Mean MCH(pg)****	17	25	15	27
Mean MCHC(gm/dl)*****	25	32	27	34
S. Iron	35µg/dL	95	35 µg/dL	100
Mean TIBC ⁺	390 µg/dL	268	350 µg/dL	270

Note : Anemic± = Hb < 10gm/dl (Normal Hb in < 2mo 9 – 14 gm/dl and > 2months 11.5-15.5gm/dl)³ MH*= Microcytic Hypochromic, NN**=Normocytic Normochromic, MCV***=Mean Corpuscular Volume (1month- 6 yrs = 76- 88(fl),⁴MCH****=Mean Corpuscular Hemoglobin (1month- 6 yrs= 24-30 (pg),⁴ MCHC*****= Mean corpuscular Hemoglobin Concentration (1month- 6 yrs=30-36gm/dl),⁴ S.Iron (infants =100-400 µg/dL and above Infancy =250-400 µg/dL)³, TIBC⁺ -Total Iron Binding Capacity (all age =22-184 µg/dL)³

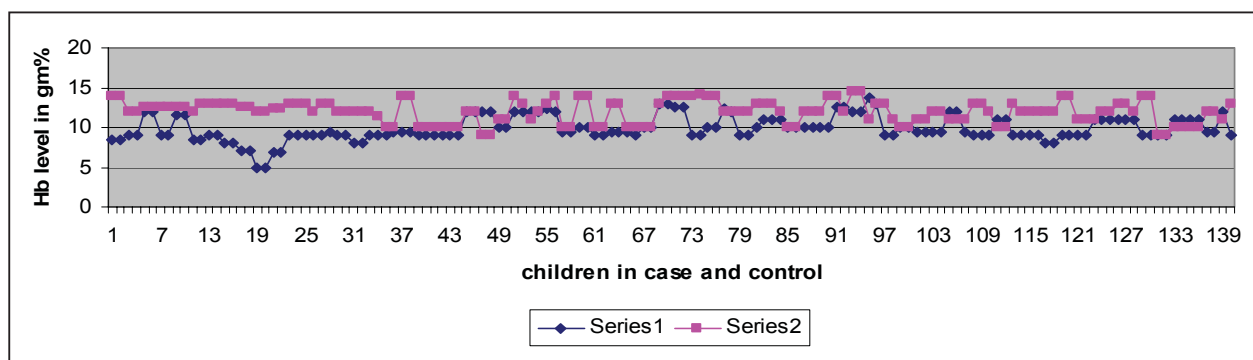


Fig. 3: Graph showing range of Hb in case and control

Table 5: Low Hemoglobin with type of ALRTI

	Bronchopneumonia (N= 72)		Wheeze associated LRTI bronchiolitis / recurrent wheezing (N= – 68)	
	Number	percentage	Number	percentage
Hemoglobin				
≤10gm%	62	86.0 %	34	50 %
>10gm%	10	13.9 %	34	50 %
Total =140	72	100%	68	100%

Table 6: Multivariate Logistic Regression Analysis Showing the Risk factor of ALRTI

Parameters	OR	95% CI	Significance
HB≤10	5.6	2.7-11.7	df=1, p<0.001
S.Iron	15.6	8.2-29.6	df=1, p<0.001
TIBC	1.7	0.86-3.4	df=1, p= 0.119

C.I: Confidence interval, OR: Odds Ratio,df:degree of freedom, LRTI- Lower Respiratory Tract Infection.

Table 7: History, Clinical finding and CXR of Mantoux positive cases.

Cases with Mantoux positive	1	2	3	4	5	6	7	8	9	10
Recurrent ARI	+	+	-	+	-	+	+	+	+	+
ESR > 50mm/1 st hr	+	+	+	+	+	+	+	+	+	+
Contact with TB	-	-	+	+	+	-	-	-	+	-
Weight loss	+	+	+	+	-	-	+	+	+	+
CXR – compatible with tuberculosis	+	+	-	-	-	-	-	-	+	+
Gastric lavage for AFB	-	-	-	-	-	-	-	-	-	-
Crofton, Horne and Miller scoring > 7	9	9	8	10	8	7	8	9	9	8

Discussion

Acute lower Respiratory tract infection (ALRTI) is a leading cause of mortality in children below 5 years of age in developing countries⁵. Hence it is important to control the risk factors to prevent deaths from ALRTI. Along with many risk factors like low birth weight, lack of breast feeding, severe malnutrition, smoke, cooking fuel⁶, low hemoglobin may also be a risk factor. Present study was carried out to prove this fact. There were 140 cases (M=99 & F= 41) and 140 controls (M=94&F=46) among which in cases maximum children were between 2month – 1 year. This signifies that ALRTI is most common in age group 2month to 1 year. This is the time when a child starts having low hemoglobin levels and also this is the period of adding supplemental feed which may be inadequate and inappropriate. The reasons for higher number of males may be gender biasness by the parents to bring them for hospital care. Sign symptoms of patient had usual presentation of ALRTI. These patients came to us only after 4-5 days of illness or when the child became more ill as with less illness people of this region do not visit hospital. Radiologically evidence of pneumonia was higher 70 (50 %) than hyperinflated lungs (bronchiolitis, recurrent wheeze) 40 (29%). This

may indicate that low hemoglobin has higher risk for pneumonia than bronchiolitis. Table 5 reveals that among pneumonia cases 86% were anemic whereas only 50% cases were anemic among bronchiolitis cases. There was no specific golden criterion to differentiate bacterial (pneumonia) or viral (bronchiolitis) ALRTI but ill looking child, CRP positive, neutrophilic leukocytosis, blood culture positive was considered bacterial infection and viral infection were assessed clinically and leucopenia was considered. Literature related to this finding was not available. It was observed that 20(50%) children with hyperinflated lung fields had a history of wheeze and 10 (25%) gave a positive family history of asthma. This maybe due to the fact that bronchiolitis is more prone to occur if there is a genetic predisposition or has a history of Atopy rather than low hemoglobin. These population was not excluded from the study as they had features of secondary infection clinically with high fever, ill looking, not feeding well and biochemically with either neutrophilic leukocytosis or CRP positive. Blood culture showed growth in only 10 % of cases and *klebsiella* was most common (4.2%) organism isolated. In this study Hb ≤ 10gm/dl was considered anemia (Normal Hb =

<2mo 9-14gm/dl and > 2months -11.5 – 15.5gm/dl)³. Mean Hb level in this study was 9.58 gm% for cases & 12gm% for Control group. Ramakrishnan K, Harish PS in their study found that anemic children were 5.75 times more susceptible to LRTI⁷ which was 3.2 times in this study. Several risk factors for developing ALRTI had been reported in different studies. Baskaran et al⁸ in their study in children between 3-5 years had found 83% with pneumonia had hemoglobin less than 11 g/dL. In this study microcytic and hypochromic picture was seen in maximum children (82.3%). In another study of iron deficiency anemia and respiratory infection by De-Silva A et al⁹, an over all prevalence of anemia was found in 52.6%. The role of low hemoglobin level per se, as a risk factor for developing ALRTI are reported only in few literatures⁷. They had found that reduced hemoglobin level due to whatever etiology was a significant risk factor for developing ALRTI. Unlike those studies here it was found that low hemoglobin due to Iron deficiency anemia was the main cause for ALRTI. Iron deficiency anemia was detected based on low MCV(normal=76-88 fl), low MCH(Normal=24-30 pg), low MCHC(Normal=30-36gm/dl), low S.Iron [Normal=infants 100-400 µg/dL and above Infancy 250-400 µg/dL] and increased TIBC[Normal =all age=22-184 µg/dL]. Serum ferritin level was not done due to unavailability of this test and ferritin level is not reliable in cases with infection as it increases probably as acute phase protein¹⁰. If you look at the normal function of Hemoglobin it facilitates oxygen (O₂) and carbon dioxide (CO₂) transport. It carries and inactivates nitric oxide (NO) and also play the role of a buffer¹¹. Hemoglobin in the blood is mainly responsible for stabilizing the oxygen pressure in the tissues¹². Therefore quantitative and/or qualitative reduction in Hb, may adversely affect the normal functions. Iron is principally required for haemoglobin synthesis.¹³ Intestinal iron absorption is related to erythropoietic requirements, although the regulatory mechanism(s) remain unknown. The usual source of iron in the lung is serum iron which is derived from catabolised erythrocytes and absorbed iron¹³. Probably it may be the reason for low hemoglobin level found to be as a serious risk factor for developing ALRTI. Further studies including other risk factors like low birth weight, lack of breast feeding, severe malnutrition, smoke, cooking fuel etc along with low hemoglobin should be considered as future perspective.

Conclusion

To conclude Hb was a risk factor for LRTI ($p < 0.001$). Iron deficiency anemia was the main cause detected. Anemia was responsible for pneumonia more than bronchilitis. Iron supplementation in age group 1 month to 5 years may reduce the incidence of LRTI and prevention

of anemia, due to whatever etiology is also essential. The limitation of this study is that other variables were not considered in this study. It is difficult to correlate the one point prevalence of pneumonia with anaemia as the control group could present with pneumonia within another few months. Only way to see is to follow a group of children with normal and low haemoglobin over a period of time for an episode of pneumonia.

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Conflict of Interest: None

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