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Correlation of Serum Iron Levels with Acute Lower Respiratory Tract Infections in Children

[1]Sheikh Quyoom Hussain, [2]Imran Ahmad Gattoo, [3]Roshi Bhagat,
[4]Naveed Shahzad, [5]Juvera Gull Wani

I. Introduction

Lower Respiratory Tract Infections (LRTI) includes all infections of the lungs and the airways below the larynx.[1] Acute lower respiratory tract infections are the leading cause of death in children below 5 years of age.[2]On an average children below 5 years of age suffer about 5 to 6 episodes of LRTI per year.[3,4]ALRTI includes croup syndromes, bronchitis, bronchiolitis and pneumonia.[5]

Pneumonia is the biggest single cause of childhood death under the age of 5 years in developing countries.[6] Approximately 150 million episodes of childhood pneumonia are reported every year from the world out of which 95 percent are from developing countries. Fifteen countries account for nearly 75 percent and six countries including India account for 50 percent. India alone bears the burnt of 40 percent disease burden. Globally there are about 3 million deaths, less than 5 years of age, each year due to pneumonia, of these deaths 90-95% are in the developing countries.[7] In India, recent estimate in under-five suggest that 13% of deaths and 24% of national burden of disease is due to pneumonia.[8] Hospital based studies have reported that 20-30% of admissions in under-five are due to pneumonia. Case fatality rates in hospitalised children are reported to be between 8.7-47%.[9,10,11,12]

Various interventions like the Acute Respiratory Infection (ARI) Control programme, by WHO have been done to reduce pneumonia related morbidity and mortality.

The haemoglobin (Hb) molecule is a tetramer formed by four polypeptide chains, two α-chains (141 a.a long)[13] and two β-chains (146 a.a long)[14,15] and has a total molecular mass of 64.5kd. Each of these chains is attached to a prosthetic group heme formed by protophyrin IX and complexed with an iron molecule.

Hb carries oxygen from the lungs to the capillaries and carbon dioxide in the reverse direction. In addition humans need to adapt to sudden changes in oxygenation requirements, therefore require modulation of the o_2 carrying capacity of haemoglobin.

LRTI associated with anemia occur more commonly in children than in adults, with anemia affecting approximately 30% of children all over the world.[16,17]

National Family Health Survey (NFHS)-3 data shows that 7 out of every 10 children age 6 to 50 months in India are anemic. Three percent of children age 6 to 59 months are severly anemic (Hb <7.0 g/dl), 40 percent are moderately anemic (Hb 7.0-9.9 g/dl), and 26 percent are mildly anemic(10.0-10.9).[18] Anemia among children is widespread throughout India. The prevalence of anemia varies from 38% in Goa to 78% in Bihar. More than half of young children in 24 states have anemia including 11 states where more than two-thirds of children are anemic. A prevalence rate of over 65% in preschool children has been reported in various studies undertaken in rural and urban India.

Iron deficiency is the most frequent and widespread nutritional deficiency in the world. In fact, iron deficiency is the only micronutrient deficiency that is also prevalent in virtually all developed countries.[19] Iron deficiency affects nearly 2170 million persons worldwide, and 1200 million of them are anemic, of which 90% are in the developing countries.** The development of iron deficiency is a result of the interaction between iron intake, physiologic iron requirements and the potential for blood loss. Much of the world's population eat little or no meat, with their nutrition derived from cultivated grasses such as rice, which are poor sources of iron,[20] which contributes to the fact that iron deficiency is the most common nutritional anemia worldwide.

II. Material And Methods

Study Design

The present study was a hospital based prospective study conducted over a period of one year from February 2012 to March 2013, in the Department of Pediatrics, G.B Pant Hospital, a tertiary care hospital which is an associated hospital of Government Medical College Srinagar.

Sample Size

The predetermined prevalence of anemia among lower respiratory tract infections in children in study and control groups was 68.6% and 21.8% respectively. We choosed a power of 90% at 95%

confidence interval, the sample size for current study was 90 cases in each group. However the ethics committee suggested to take 110 cases in each group for convenience and more accuracy.

Inclusion Criteria for cases in study group:
The inclusion criteria for cases were as per WHO criteria for LRTI.

- Fever
- Cough
- Fast respiratory rate
- Chest in-drawing
- Ronchi or crepitations on auscultation

Exclusion Criteria
The exclusion criteria were children suffering from other systemic illnesses:

- Congenital heart diseases.
- Tuberculosis (any evidence plus Montaux test positive cases).
- 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.

Hemoglobin level <10gm% was considered low in this study.
110 cases satisfying the both inclusion as well as the exclusion criterias were taken in the study group. Age and sex matched children not having respiratory problems were taken as controls.

The cases in both study as well in the control group were subjected to intensive investigations which included:

- Complete blood count (CBC).
- Peripheral blood smear.
- Blood culture and sensitivity test.
- X-ray chest.
- Serum iron and iron binding capacity.

Blood sample were taken from anti-cubital vein of each child by a trained phlebotomist. Sterile, disposable syringes and needles, and proper tubes were used. Haemoglobin level was estimated in the blood samples using cyanmeth method by automatic blood cell analyser. Iron level and TIBC were measured by using the Ferrozine method without deprotienization.

III. Statistical Analysis

Data was described as mean ± SD/SE and percentages. Least significant difference for intergroup variance was measured at 95% confidence interval. The metric data was analysed by student's t-test whereas Man-Whitney U test and Fisher's exact test were used for non-parametric data. p-value was expressed upto three decimal places. SPSS 19.0 and Excel software were used for data analysis.

Observation And Results:

Table-1

Age (months) distribution of the studied subjects						
		Study (110)		Control (110)		p value
		n	%	n	%	
Age (month)	≤ 2	13	11.8	10	9.1	0.435 (NS)
	3 to 23	**89**	**80.9**	**90**	**81.8**	
	24 to 59	8	7.3	10	9.1	

Table-2

GENDER DISTRIBUTION OF STUDIED SUBJECTS						
		Study (110)		Control (110)		p value
		n	%	n	%	
Gender	Male	63	57.3	65	59.1	0.785 (NS)
	Female	47	42.7	45	40.9	

Table-3

P.B.F. Results of Anemic subjects						
		Study (110)		Control (110)		p value
		n	%	n	%	
Anemia		**71**	**64.5**	**31**	**28.2**	0.001 (Sig)
P.B Smear	Hypochromic Microcytic	**56**	**78.9**	**10**	**32.3**	0.001 (Sig)
	Normocytic Normochromic	**15**	**21.1**	**21**	**67.7**	

Table-4

CLINICAL FEATURES IN THE STUDIED SUBJECTS					
	Study (110)		Control (110)		p value
	n	%	n	%	
Fever	**104**	94.5	91	82.7	0.006 (Sig)
Cough	**110**	100.0	8	7.3	0.000 (Sig)
Fast Respiratory Rate	**74**	67.3	0	0.0	0.000 (Sig)
Chest in-drawing	**92**	83.6	0	0.0	0.000 (Sig)
Ronchi or Crepitation on Auscultation	**64**	58.2	0	0.0	0.000 (Sig)
Vomiting	23	20.9	**56**	50.9	
Diahorrea	6	5.5	**38**	34.5	
Pain Abdomen	3	2.7	**32**	29.1	
Dehydration	6	5.5	**30**	27.3	
Convulsions	9	8.2	28	25.5	
Other Non-respiratory Symptoms(Poor Feeding,Irritability,Sore Throat)	60	54.5	66	60.0	

In the study group, anemia (haemoglobin <10 g%) was present in 71 (64.5%) cases while in the control group anemia was found in 31 (28.2%). The p-value is 0.001, which is significant.

Table-5

ANEMIA IN THE STUDIED SUJECTS					
	Study (110)		Control (110)		p value
	n	%	n	%	
Anemia	**71**	**64.5**	**31**	**28.2**	0.001 (Sig)

In peripheral blood film , hypochromic microcytic picture was seen in 56(78.9%) cases in the study group and 10(32.3%) cases in the control group while as normocytic normochromic picture was seen in 15(21.1%) cases in the study group and 21(67.7%) cases in the control group.

Table-6

Graphical Representation Of P.B.Smear Results In Anemic Subjects

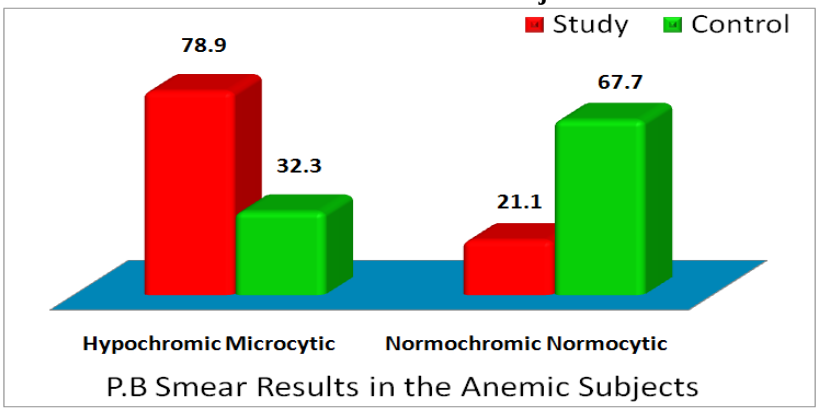

Table -7

SERUM IRON LEVEL IN THE STUDIED SUBJECTS				
		Anemia	Normal	p value
Study	Serum Iron (mcg/dl)	**35.3 ± 14.4** (19, 72)	**57.1 ± 13.8** (34, 81)	0.000 (Sig)
Control	Serum Iron (mcg/dl)	**52.4 ± 15.1** (34, 84)	**62.6 ±16.7** (35, 95)	0.004 (Sig)

In the study group, the mean serum iron level was 35.3 mcg/dl in the anemic cases and 57.1 mcg/dl in the non-anemic cases. p-value was (0.000) which is significant. In the control group, the mean serum iron level was 52.4 mcg/dl in the anemic cases and 62.6 mcg/dl in the non-anemic cases. p-value was (0.004) which is significant.

Table-8

Graphical Representation Of Serum Iron Level Among Studied Subjects

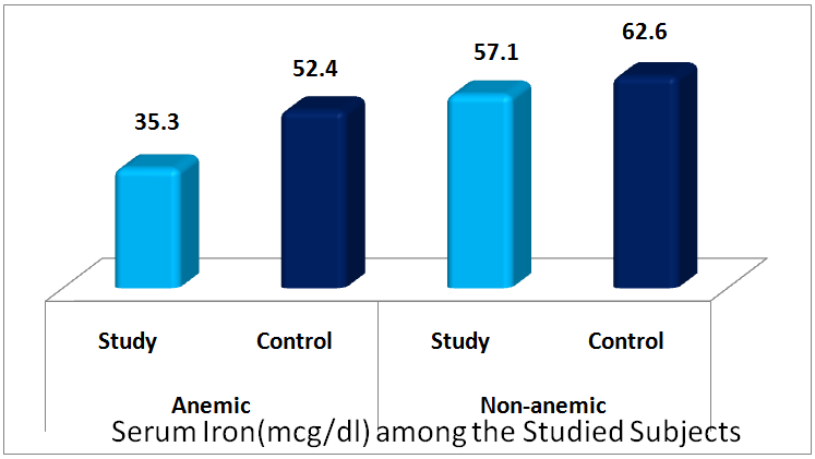

Table -9

SERUM TIBC (mcg/dl) LEVEL IN THE STUDIED SUBJECTS				
		Anemia	Normal	p value
Study	TIBC (mcg/dl)	429.3 ±41.9(296,495)	389.9 ±58.5(296,498)	0.000 (Sig)
Control	TIBC (mcg/dl)	409.1 ±61.5(301,495)	368.6 ±51.4(290,499)	0.001 (Sig)

Serum TIBC, infants=100-400 mcg/dl, above infancy=250-400mcg/dl[48(b)]

In the study group, the mean serum TIBC level in anemic cases was 429.3 mcg/dl, and 389.9 mcg/dl in the non-anemic cases. p-value was (0.000), which is significant. In the control group the mean TIBC level in anemic cases was 409.1 mcg/dl and 368.6 mcg/dl in the non-anemic cases. p-value was 0.001 which is significant.

Table-10

Graphical Representation Of Tibc Level In The Studied Subjects

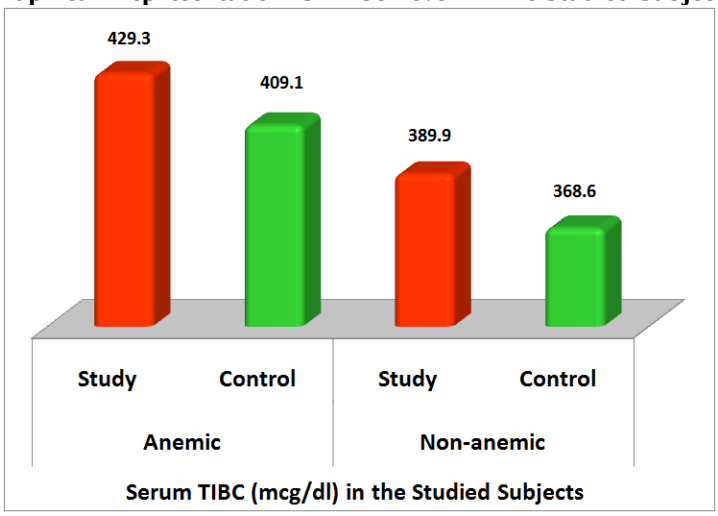

Table-11

Comparison between Study and Control groups			
	Study	Control	p value
Age (month)	9.7 ±0.9(1,58)	11.5 ±1.1 (1,59)	0.203 (NS)
Hospital Stay (day)	5.0 ±1.5(3,10)	5.1 ±1.4(3,7)	0.784 (NS)
Hemoglobin (gm%)	**8.8 ±1.6 (6.4 , 12.5)**	**11.6 ± 1.7 2(8,12.7)**	**0.000 (Sig)**
Total Leucocyte Count (000,s)	10.4 ±2.4(6.6,15.5)	10.3 ±2.5(6.5,14.6)	0.776 (NS)
DLC_P	61.0 ±5.1(50,77)	60.6 ±4.1(52,69)	0.540 (NS)
DLC_L	33.4 ±4.7(20,45)	33.4 ±3.8(23,40)	0.975 (NS)
DLC_M	4.7 ±1.9(2,8)	4.9 ±1.9(2,8)	0.443 (NS)
DLC_E	1.0 ±0.9(0,2)	1.1 ±0.8(0,2)	0.155 (NS)
Serum Iron (mcg/dl)	**43.0 ± 17.6 (19,81)**	**59.6 ±17.0(30,95)**	**0.000 (Sig)**
TIBC (mcg/dl)	**415.3 ±51.8(296,498)**	**380.0 ±57.1(290,499)**	0.000 (Sig)

IV. Discussion

The present study was a hospital based prospective study conducted over a period of one year from February 2012 to March 2013, in the Department of Pediatrics, G.B Pant Hospital, which is an associated hospital of Government Medical College Srinagar.

Acute Lower Respiratory Tract Infection (ALRTI) is a leading cause of mortality in children below 5 years of age in developing countries.[21]

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 breastfeeding, severe malnutrition, smoke, cooking fuel[22], low haemoglobin is also be a risk factor. Present study was carried out to study the correlation between serum iron levels and acute lower respiratory tract infection in children.

There were 110 cases (M=63 & F=47) in the study group and 110 cases (M=65 & F=45) in the control group. In our study, 57.3% were males and 42.7% were females in the study group and 59.1% were males and 40.9% were females in the control group. In Malla et al [23] 70.7% were males, 29.3% were females in the study group and 57.3% were males and 42.3% were females in the control group. The reasons for a slightly higher number of males may be the gender bias by the parents to bring them for hospital care. In Malla et al[23], 49.2% children were in the age group of 2 month to 1 year. In our study, the maximum number of children were also between 3 months and 23 months both in the study (80.9%) as well as in the control (81.8%) group. This signifies that ALRTI is most common in age group 3 months to 23 months. This is the time when a child starts having low haemoglobin levels and also this is the period of adding supplemental feeds which may be inadequate & inappropriate . The patients in the study group had usual presentation of ALRTI. .

In this study haemoglobin level <10 gm% was considered low. Mean Hb level was 8.8 gm% in the study group and 11.6 gm% in the control group. In Malla et al[23], the mean Hb level was 9.58 gm% in the cases and 12 gm% in the control group.

Anemia was found in 71 (64.5%) cases in the study group and in 31 (28.2%) cases in the control group. In Malla et al[23], anemia was found in 96 (68.6%) cases in the study group and 30 (21.42%) cases in the control group. In Ramakrishnan et al[25] anemia was found in 74 (74%) cases in the study group and 33 (33%) cases in the control group.

In De-Silva et al[26] an overall prevalence of anemia was found in 52.6% cases.

In our study, 65.1 % males and 63.8 % females were anemic in the study group, 27.7 % males and 28.9 % females were anemic in the control group. Similar results with no significant gender difference in anemic children were also found by Mourad et al[27] in children less than 5 years of age with lower respiratory tract infections.

Anemic patients were found to be 4.6 times more susceptible to ALRTI in our study. Ramkrishnan et al[25] found that anemic children were 5.75 times more susceptible to ALRTI while as Malla et al[23] found that they were 3.2 times more susceptible to ALRTI. Mourad et al[27] found that anemic children are twice more susceptible to lower respiratory tract infections as compared to non-anemic children.

In our study hypochromic microcytic anemia was seen in 78.9% of total anemic cases in the study group. In Baskaran et al[24] it was found in 82.3% cases.

Iron deficiency was found in 78.9% of total anemic cases in the study group. Malla et al[27] found iron deficiency in 82.3% cases.

The role of low Hb level per se, as a risk factor for developing ALRTI are reported only in few literatures. They had found that reduced Hb level due to whatever etiology was a significant risk factor for developing ALRTI. Here in this study low haemoglobin due to iron deficiency was found

the main cause of ALRTI. Malla et al[23] has also founded low Hb due to iron deficiency was the main cause of developing ALRTI.

Hb facilitates oxygen (o_2) and carbon-dioxide (co_2) transport. It carries and inactivates nitric oxide (NO) and also plays the role of a buffer.[28]

Hemoglobin in the blood is mainly responsible for stabilising the oxygen pressures in the tissues. Therefore quantitative and/or qualitative reduction in Hb, may adversely affect the normal functions. Iron is primarily required for haemoglobin synthesis. Intestinal iron absorption is related to erythropoietic requirements, although the regulatory mechanisms remain unknown. The usual source of iron in the lungs is serum iron which is derived from catabolised erythrocytes and absorbed iron. 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 breastfeeding, severe malnutrition, smoke etc along with low Hb should be considered a future prospective.

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