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Original Article

Acute Lower Respiratory Tract Infections

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ASSOCIATION OF IRON DEFICIENCY ANEMIA WITH ACUTE LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN PRESENTING TO PEDIATRICS DEPARTMENT OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To establish association between acute lower respiratory tract infection and iron deficiency anemia.
Study Design: Case-control study.
Place and Duration of Study: Pediatrics Department, Pak Emirates Military Hospital, Rawalpindi, from Dec 2017 to May 2018.
Methodology: A total of 100 children with age ranging from 6-60 months were selected for this study with 50 being in each group. Study group constituted of children presenting with acute lower respiratory tract infection and healthy children presenting to outpatient were taken as controls. Hemoglobin levels (<11g/dl), mean corpuscular volume (<70fl), Serum Ferritin (<30ng/ml) and red blood cell Morphology were used to determine iron deficiency anemia. Patients meeting the WHO criteria were labeled to have acute lower respiratory tract infection.
Results: The frequency of iron deficiency was found to be 40 (80%) in cases and only 34 (17%) in healthy controls. A significant association was found between iron deficiency anemia and acute lower respiratory tract Infection with an odds ratio of 7.76 and a significant *p*-value of <0.01.
Conclusions: Iron deficiency anemia has an increased association of up to seven times in children with acute lower respiratory tract infections as compared to healthy children thus highlighting it as a significant risk factor.

Keywords: Acute lower respiratory tract infection, Hemoglobin, Iron deficiency anemia, Pneumonia.

INTRODUCTION

Acute lower respiratory tract infections form a major portion of early childhood illnesses and infections. Acute lower respiratory tract infection (ALRTI) is characterized by inflammation of respiratory airways below larynx till lung parenchyma[1]. Amongst them, pneumonia is the major killer accounting for 18% of under 5 year children mortality every year, according to World Health Organization (WHO)[2]. A Global Action Plan for Prevention and Control of Pneumonia (GAPP) has been devised by WHO with goal to reduce pneumonia-associated early childhood deaths to as few as 3 per 1000 live births every year by 2025[3].

Anemia is defined as a hemoglobin level of less than 11 g/dl for age group <5 yrs and that less than 12 g/dl for up to 12 yrs of age[4]. About, 61.9% of children belonging to the age group <5 years are suffering from anemia. Up to 53.7% of children are anemic in Pakistan amongst which 28.6% have Iron-deficiency anemia in our region of Pakistan[5]. A number of causes are attributable to iron deficiency such as poor dietary intake, microscopic blood loss and malabsorption. Iron deficiency anemia (IDA) is associated with a number of comorbid and complications such as easy fatigability, poor growth and brain development, poor mental health, cardiorespiratory compromise and increased susceptibility to infections.

The laboratory parameters that can be used to assess iron deficiency anemia may include mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), hematocrit (Hct), mentzer's index, serum ferritin levels, serum transferrin saturation, serum iron levels and serum total-iron binding capacity (TIBC) and red cell distribution width (RDW). Age based cut-off values for each parameter is set. Serum ferritin levels are one of the best markers of iron stores, being the first one to be affected in iron-deficiency, add to the sensitivity of test.

Iron has a crucial role in functioning of iron proteins such as hepcidin, lactoferrin, haptoglobin, and transferrin. These proteins help in building up the innate immunity[6]. Thus, in cases of iron deficiency there is an inadequate immune response and an increased risk of acquiring infection particularly in children <5 years who are more prone to Iron deficiency and thus anemia. This present study was directed towards finding an association of iron deficiency anemia and acute lower respiratory tract infections. The study results would help us in better understanding of iron deficiency anemia as a risk factor for ALRTI and timely

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interventions would help us prevent acute lower respiratory tract infections.

METHODOLOGY

We conducted a case-control study to look for association between IDA and ALRTI in children with age range of 6-60 months. The study was carried out at Pediatrics department of Pak Emirates Military Hospital, Pakistan, from December 2017 to May 2018. Sample size was calculated using online openepi software using Odds Ratio (OR) of 3.59[7], and percentage of cases with exposure was 70.53. A total of 100 subjects were enrolled through consecutive sampling; which included 50 cases; presenting with acute lower respiratory tract infections and 50 healthy controls. All children belonged to age group ranging from 6-60 months however, they were selected without any preference for age group, gender and vaccination status.

Cases were those admitted indoor patients through outpatient or emergency with signs and symptoms of lower respiratory tract infections. They were classified on the basis of severity of symptoms based on WHO classification of Cough or Difficult breathing.

Patients selected as controls only included those children who were presenting to outdoor for routine well child checkup and did not have any symptom of acute lower respiratory tract infection in specific or any other infection in general.

Children with any underlying chronic disease such as immune deficiencies, congenital heart disease, congenital chest deformities, tuberculosis, diabetes, cystic fibrosis, bronchiectasis and allergic disorders were excluded from our subjects; both cases and controls.

Ethical committee's permission was taken before beginning research sampling. The purpose of study was explained to the patients before enrolling them as subjects. The purpose of study was explained to the patients before enrolling them as subjects. An informed consent was taken from parents/guardians.

Blood samples were withdrawn after taking informed consent from mothers. Blood investigations performed to look for iron deficiency anemia included complete blood count (CBC), red blood cell (RBC) morphology, MCV and Serum Ferritin. A minimum of 1ml each of blood sample was sent in EDTA bottle and Plain bottle for CBC & morphology and serum ferritin respectively.

Patient was labelled to have iron deficiency anemia on the basis of following criteria; 1) A hemoglobin level of <11 g/dl, 2) lowest cut off value for serum ferritin was <30 ng/ml, 3) RBC Morphology showing hypochromia, microcytosis, anisocytosis, or pencil cells[4].

Acute lower respiratory tract infections included Acute Laryngitis, Acute Bronchitis, Acute Tracheitis, Croup, Acute Bronchiolitis and Pneumonia. ALRTI was diagnosed clinically with aid of WHO/IMCI classification of Cough or Difficult breathing by assessing respiratory rate, looking for chest in-drawing, nasal flaring and subcostal recessions and listening for stridor and wheeze. Following is the elaboration of classification of Cough or difficult breathing on the basis of World Health Organization (WHO)[8]. Child was classified as 1) Cough or cold; when there were no signs of pneumonia or very severe disease, 2) Pneumonia; when there was fast breathing or tachypnea for age (6 months 12 months: 50 breaths per minute or more, 12 months 60 months: 40 breaths per minute or more) and/or subcostal recessions or nasal flaring, 2), very severe disease or severe pneumonia; when there is stridor in a calm child or when all signs of pneumonia are visible and danger signs are present including lethargy, poor oral intake, vomits everything, seizures or history of seizures in this illness.

IBM Statistical Package of Social Sciences (SPSS) version 21 was used for data analysis. Results were analyzed by frequency, percentages, mean and standard deviation. To compare the relation of the results and comparison of means; independent t-test and chi-square test was applied. The Odds ratio was used to compare the anemia amongst the two subject categories. The *p*-value of ≤0.05 was considered statistical significance.

RESULTS

A total of 100 children amongst which 50 presented with ALRTI (case group) and 50 children were healthy controls. In children selected as controls, 18 (36%) children belonged to 6-12 month age group, 8 (16%) to 13-24 month, 3 (6%) in 25-36 month, 9 (18%) to 37-48 month and 12 (24%) in 48-60 month age group. In this healthy control group, 27 (54%) were male and 23(46%) children were female. Out of these controls, 10(37.03%) of the boys and 7 (30.43%) of the girls had IDA.

In our case group, 23 (46%) children were in 6-12 mo age range, 8 (16%) in 13-24 mo range, 8 (16%) in 25-36 mo group, 5 (10%) in 37-48 mo and 6 (12%) in 48-60 months age group. Amongst them, 32 (64%) were male and 18 (36%) were female children. Out of these 18 (36%) girls with ALRTI (case group), 15 (83.3%) had IDA and that amongst boys, 25 (71.8%) had IDA.

The average hemoglobin levels (p=0.03) amongst cases were 9.7 ± 6.1 g/dl which are significantly low. Similarly, hemoglobin levels (p-value= 0.05) in healthy group were found to be around 11.1 ± 3.9 g/dl which are significantly higher (table-I).

Six (33.33%) of the children in 6-12 months age group of control, 4 (50%) of 13-24 month age group, 1 (33.3%) of 25-36 month age group, 4 (44.4%) of 37-48 month and 2 (16%) children in 49-60 months age group had IDA (fig-1).

Similarly, amongst the 40 (80%) subjects in case group who had IDA, a maximum of 19 (47.5%) children with belonged to the age group of 6-12 months age group followed by 7 (17.5%) in age range of 13-24 month. Amongst other age groups of cases positive for IDA, 6 (15%) of the children were in age range of 25-36 month, 3 (7.5%) of children from 37-48 month and 5 (12.5%) of children in age group of 49-60 month (fig-2).

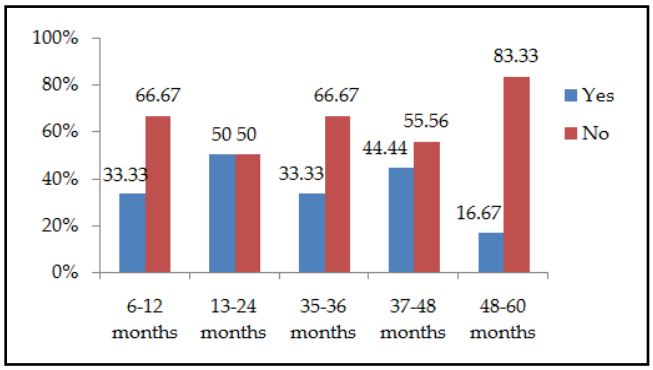

Figure-1: Age wise distribution of frequency of iron deficiency anemia in healthy group.

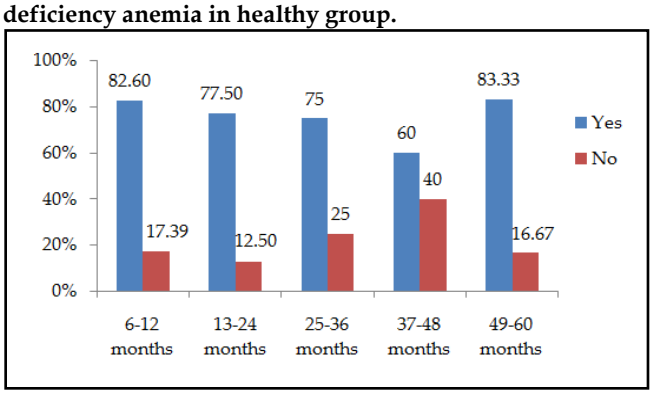

Figure-II: Age wise distribution of frequency of iron deficiency anemia in children with acute lower respiratory tract infection.

The overall incidence of IDA amongst children presenting with ALRTI was 40 (80%); out of which 25 (62.5%) were Males and 15 (37.5%) Females and only 17 (34%) children in control group had IDA of which 10 (58.8%) were males and 7 (41.1%) were Females. In study group, male formed a 62% of the total children with IDA and in control group 58.8% of the children with IDA were males showing an increased incidence of IDA in male children.

For patients with ALRTI, Odds Ratio was found to be 7.7 with a confidence interval of 3.1-19.2 which shows iron deficiency Anemia as a significant risk factor as shown in table-I. Thus, a significant interaction was found amongst iron deficiency anemia and acute lower respiratory tract infections with a p-value of <0.01 as shown in table-II.

Table-I: Iron deficiency anemia as a strong risk factor for acute lower respiratory tract infection.

Risk Factor	Odds Ratio	p-value	95% Confidence Interval
Anemia in Patients with ALRTI	7.7	<0.01	3.1-19.2
Anemia in Male children	6.07	<0.01	1.9-19
Anemia in Age group 6-12 month	9.5	<0.01	2.2-40.7

Table-II: Association of Iron deficiency anemia with acute lower respiratory tract infection.

Baseline Characteristics	Study Groups		p-value
	Patients with ALRTI	Healthy Group	
Anemia	40 (80%)	17 (34%)	0.01
No Anemia	10 (20%)	33 (66%)	

DISCUSSION

Iron deficiency is a leading risk factor for anemia in children. About 150 million episodes of childhood pneumonia are reported every year worldwide out of which 10 million cases occur in Pakistan[9]. Every year globally 0.9 million children die due to pneumonia and out of which 80% children are under the age of 5 years[10]. Our study showed a statistically significant relation between iron deficiency anemia and LRTI in children belonging to age range of 6 months to 5 years with majority of them falling below 1 year of age.

A hemoglobin level of <11 g/dl, an MCV of <75fl and a serum ferritin level of <30 ng/ml was taken as a criteria to diagnose iron deficiency anemia[11]. According to the results of our study; 80% of the children in cases group and only 34% of control group had IDA. A similar study was conducted in Nepal on 200 children of a tertiary hospital in the year 2015. According to this study, a total of 86% of study group were found to have iron deficiency anemia[12]. Another study conducted in Nepal over 200 children in the year 2018 showed

up to 2.68 times more susceptibility of LRTI in children with IDA[13].

A study conducted in India on a limited sample size did not show a significant statistical relation of iron deficiency anemia with children presenting with wheeze associated respiratory tract infections[14]. Another study was carried out at a hospital in Mumbai in 2016, which also disclosed a significant association between Pneumonia and IDA with an Odds Ratio of 3.59[7].

Iron deficiency anemia was also studied as a risk factor in children presenting with Pneumonia at a tertiary care hospital setup in Egypt in 2015. According to that study, Children with IDA had four times more susceptibility of acquiring pneumonia then control children without IDA[15]. It also studied the possibility of recurrent chest infections in children IDA which was also found to be higher. Our current study also showed a statistically significant result with an odds ratio of 7.76. It also revealed a statistically significant rise in IDA in children with ALRTI having an average hemoglobin level of 9.7 ± 6.1 g/dl and amongst controls the range was found to be 11.19 ± 3.9 g/dl. These difference in Hb levels of both groups of our study were comparable with a study conducted in Egypt where Hb levels were statistically significantly decreased (11.40 ± 0.40 g/dl) in cases in comparison to control group (12.07 ± 0.50 g/dl)[6].

Another cross sectional case-control trial was performed on children belonging to Nepal with age ranging from 6 months to 5 years over a time period of one year. They also used WHO criteria for diagnosing LRTI in children[16]. This trial also revealed an increased incidence of IDA in children being diagnosed with LRTI with an almost equal susceptibility of 4.99 times as that observed in another Egyptian trial[17]. Another recently conducted Egyptian study showed an iron deficiency anemia in 55% of the children belonging to study group as compared to controls with only 27.5% anemic children[18]. Our study also showed similar results and a possible greater linkage, with a 7.7 times more susceptibility of IDA in children with ALRTI.

Hence timely measures should be taken through education of community masses regarding prevention of iron deficiency. Earlier recognition and timely intervention will help decrease the various complications associated with it. The limitation of this study is small sample size and duration. In order to get more reliable data it is recommended to perform more studies but with a bigger sample size.

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CONCLUSION

Children with ALRTI had an increased association of upto 7.7 times more with IDA. This study showed that IDA is a significant risk factor for ALRTI. The total incidence of IDA was 57% (57) when subject for cases and control groups were combined.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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