

Evaluation of Anemia as a Risk Factor for Lower Respiratory Tract Infection in Children

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ABSTRACT

Background: Acute lower respiratory tract infection being a leading cause of death in children less than five years of age and anemia is the commonest cofactor in these patients seeking medical advice, particularly in developing countries.

Aim: To determine the association of anemia with lower respiratory tract infection in children by evaluating the frequency of anemia in children with and without LRTI.

Methods: A Case Control Study was carried out at department of Pediatrics, Children hospital Lahore, Institute of child health from 20-1-18 to 20-7-19. Blood was drawn by phlebotomist from each patient included in this study by using disposable and sterile syringes and accurate tubes. Blood samples were used to estimate hemoglobin level by using automatic blood cell counter. Anemia was defined as per operational definition. Children were managed as per standard protocol.

Results: In this study risk of anemia was significantly higher among cases i.e. Cases: 54% & Controls: 22%, OR= 4.162, p-value=0.001. Although in all age groups frequency as well as risk of anemia was higher in cases. But children among cases in the elder age group showed statistically significant risk for anemia as compared to children in control group i.e. 31-45 Months. OR= 14.00, p-value=0.013 & 46-60 months: 5.60, p-value=0.027.

Conclusion: Children presenting with LRTI possesses significant risk for anemia. Thus, early and accurate diagnosis of anemia in children and treatment of anemia will have a positive effect decreasing pneumonia in children.

Keywords: Anemia, Lower respiratory tract infection, Children, association, odds ratio

INTRODUCTION

All the infections of the lungs and airway below the larynx like, pneumonia, Bronchiolitis and croup syndromes are included in lower respiratory tract infections¹. In children under five years of age acute lower respiratory tract infections are the leading causes of morbidity and mortality worldwide.² In young children it has been estimated that approximately 156 million of pneumonia occur annually with more than 10 million cases only in Pakistan, resulting in 1.4 million deaths approximately, of these approximately 95% deaths in developing countries^{2,3}. For development of lower respiratory tract infections a number of risk factors have been found, Some of them being definite, some likely and few possible. Anemia is a likely risk factor for this major source of morbidity and mortality among the children being inconsistently associated with LRTI⁴.

In developing countries Anemia is a major public health problem with an estimated 3.5 billion anemic people and can occur at any age, but is more prevalent in younger children⁵. In children Anemia is of particular concern because it affects physical, Mental and social development and results in adverse behavioral and cognitive effects leading to poor school performance and work capacity in later years⁶. In developing countries an estimated 80% children will be anemic at some point by the age of 18 years old⁷.

This study will be a significant contribution as lower respiratory tract infection associated with anemia occurs more frequently in children than adults with Anemia between age of six months and three years, during this period of age when repeated infections occur.^{7, 8} The present study will help in clarifying the role of anemia as a risk factor for LRTI in children in Pakistan which is not currently known. It is necessary to address this association because it is a modifiable risk factor of lower respiratory tract infection this may help in reducing the burden of disease⁷.

The rationale of present study is that there is no study from Pakistan which has studied the role of anemia on frequency of LRTI in children. Furthermore, the international studies report a wide range of results reporting odds ratio ranging from 2.08 to 5.78

and data is inconclusive with some studies reporting association of anemia with LRTI while others reporting no significant association⁷⁻¹⁰.

Hussain SQ et al⁹ reported frequency of LRTI of 64.5% in children with anemia compared with 35.5% in those without anemia. Malla et al⁸ found these rates to be 68.6% in anemic children versus 31.4% in children with normal hemoglobin levels whereas Mourad et al⁷ report this to be 68% and 32% respectively in anemic and non-anemic children. This study is therefore designed to be carried out at a tertiary care center with adequate sample size to determine the frequency of anemia in children with and without LRTI. Despite the significant health burden related to these two major public health problems, there have been few studies evaluating the impact of anemia on frequency of LRTI in children with inconsistent results^{7,10}.

In addition, studies are retrospective¹⁰ and have used inconsistent anemia definitions. None of the studies have used the WHO criteria for defining LRTI⁷. The studies on etiology and risk factors of LRTI from Pakistan have focused mainly on traditional risk factors e.g., low birth weight, lack of breast feeding, malnutrition. There is no study found in literature from Pakistan evaluating association of anemia as a possible risk factor for Lower Respiratory Tract Infections¹¹.

The objective of the study was to determine the association of anemia with lower respiratory tract infection in children by evaluating the frequency of anemia in children with and without LRTI.

MATERIAL & METHODS

A Case Control Study carried out at Department of Paediatric, University of Child Health, Children Hospital, Lahore. The duration of study was 6 months, i.e., from 20-1-2018 to 20-7-2019 after permission from IRB. Sample size has been calculated to be 100 with 50 children in both groups with 95% study power and 5% level of significance expecting frequency of anemia of 64.5% in patients with LRTI and 28.2% in patients without LRTI. Non probability consecutive sampling was adopted.

Inclusion Criteria: All children of both gender with age between one month to five years having diagnosis of lower respiratory tract infections.

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Exclusion Criteria

- Children whose parents to participate in study.
- Those children with congenital chest wall malformation, prematurity, server systemic illness e.g, congenital heart diseases), chronic diseases (Tuberculosis, Hepatitis, Diabetes, Liver failure etc) patient on iron supplements and previous of infection in control group.

Cases: Hospitalized for LRTI

Controls: Healthy children

Data Collection Procedure: For this study total 100 patients between the age group of 1 month to 5 years were selected; 50 patients with lower respiratory tract infection hospitalized and 50 healthy controls children without any respiratory problem. Bio data was entered in a predesigned structured Performa. Blood sample was drawn by phlebotomist from antecubital vein of each child who were included in this study by using disposable sterile syringes and proper tubes. Hemoglobin (HB) levels were measured in each blood sample by using an automatic blood cell counter. Anemia was defined as per operational definition. Children were managed as per standard protocol.

Data Analysis Procedure: Statistical analysis was done by using SPSS version 16.in this qualitative data e.g, gender and Anemia was presented as percentages and frequencies. Quantitative data like Hemoglobin level and age was presented as means and standard deviations. In this study data was stratified for gender, age and duration of symptoms.Post stratification chi square test was employed. Association of Anemia with lower respiratory tract infection was assessed by odds ratio and p- value less than 0.5 was considered statistically significant.

RESULTS

The mean age of the cases was 30.68±15.08 months the minimum age was 5 months and maximum was 59 months where the mean age among controls was 35.25±16.25 months the minimum age was 2 months and maximum was 57 months (Table 1). Among cases there were 29(58%) male and 21(42%) females. Among controls there were 22(44%) male and 28(56%) females (Table 2). Mean duration of symptoms among cases and controls was 3.58±1.99 and 4.56±2.12 days.(Table-3). Mean Hb level among cases and controls was 10.83±1.52 and 11.70±1.32.(Table-4). Among cases 27(54%) children were anemic and among controls 11(22%) children were anemic. Frequency as well as risk of anemia was significantly higher among cases as compared to controls. i.e. Odds Ratio= 4.162, p-value=0.001(Table 5). Cases in the age group 1-15 months among them risk for anemia was 2.667 times more as compared to controls. Risk of anemia was 2.025 times more for cases who were in the age group 16-30 months old. Risk of anemia among cases who were in the age group 31-45 months old and 46-60 months old was 14.00 and 5.60 times more as compared to controls. Only in the elderly age group risk of anemia was significant. However for younger age group although risk was higher but not statistically significant.(Table-6). Stratification of gender showed that for male and female participants among cases frequency as well as risk for anemia was significantly higher as compared to controls. [Male: Case:48.3% vs. Controls: 13.6%, OR=5.911, p-value=0.009] & [Female: Case 61.9% vs. Controls: 28.6%, OR=4.063, p-value=0.020] (Table-7). Risk of anemia was higher for cases whose duration of symptoms was 1-3 days. i.e. [OR=2.321, p-value=0.169] However risk of anemia was significantly higher for cases whose duration of symptoms was 4-7 days. [OR=6.933, p-value=0.002] (Table-8)

Table 1: Age of Children (Cases & Controls)

| | Cases | Controls |
|------|-------|----------|
| N | 50 | 50 |
| Mean | 30.68 | 35.24 |
| SD | 15.08 | 16.25 |
| Min | 5 | 2 |
| Max | 59 | 57 |

Table-2: Gender of Children (Cases & Controls)

| | Cases | Controls | Total |
|--------|---------|----------|-------|
| Male | 29(58%) | 22(44%) | 51 |
| Female | 21(42%) | 28(56%) | 49 |
| Total | 50 | 50 | 100 |

Table-3: Descriptive statistics for duration of symptoms (Cases & Controls)

| | Cases | Controls |
|------|-------|----------|
| N | 50 | 50 |
| Mean | 3.58 | 4.56 |
| SD | 1.99 | 2.12 |
| Min | 1 | 1 |
| Max | 7 | 7 |

Table-4: Descriptive statistics for Hemoglobin level (Cases & Controls)

| | Cases | Controls |
|------|-------|----------|
| N | 50 | 50 |
| Mean | 10.83 | 11.70 |
| SD | 1.52 | 1.32 |
| Min | 8.5 | 9 |
| Max | 13.5 | 13.5 |

Table-5: Frequency of Anemia (Cases & Controls)

| | Cases | Controls | Total |
|-------|---------|----------|-------|
| Yes | 27(54%) | 11(22%) | 38 |
| No | 23(46%) | 39(78%) | 62 |
| Total | 50 | 50 | 100 |

Odds Ratio= 4.162 (1.744-9.935), p-value= 0.001

Table-6: Frequency of Anemia (Cases & Controls) stratified for age

| Age | Anemia | Cases | Controls | Odds Ratio | p-value |
|-------|--------|-----------|-----------|------------|---------|
| 1-15 | Yes | 4(57.1%) | 2(33.3%) | 2.667 | 0.391 |
| | No | 3(42.9%) | 4(66.7%) | | |
| 16-30 | Yes | 9(47.4%) | 4(30.8%) | 2.025 | 0.348 |
| | No | 10(52.6%) | 9(69.2%) | | |
| 31-45 | Yes | 7(58.3%) | 1(9.1%) | 14.00 | 0.013 |
| | No | 5(41.7%) | 10(90.9%) | | |
| 46-60 | Yes | 7(58.3%) | 4(20%) | 5.600 | 0.027 |
| | No | 5(41.7%) | 16(80%) | | |

Table-7: Frequency of Anemia (Cases & Controls) stratified for gender

| Gender | Anemia | Cases | Controls | Odds Ratio | p-value |
|--------|--------|-----------|-----------|------------|---------|
| Male | Yes | 14(48.3%) | 3(13.6%) | 5.911 | 0.009 |
| | No | 15(51.7%) | 19(86.4%) | | |
| Female | Yes | 13(61.9%) | 8(28.6%) | 4.063 | 0.020 |
| | No | 8(38.1%) | 20(71.4%) | | |

Table-8: Frequency of Anemia (Cases & Controls) stratified for duration of symptoms

| Symptoms | Anemia | Cases | Controls | Odds Ratio | p-value |
|----------|--------|-----------|-----------|------------|---------|
| 1-3 | Yes | 15(51.7%) | 6(31.6%) | 2.321 | 0.169 |
| | No | 14(48.3%) | 13(68.4%) | | |
| 4-7 | Yes | 12(57.1%) | 5(16.1%) | 6.933 | 0.002 |
| | No | 9(42/9%) | 26(83.9%) | | |

DISCUSSION

Anemia is more prevalent in developing countries in comparison to developed countries with prevalence of 44 to74% in children⁷. The most common cause of anemia is iron deficiency anemia¹². In Nepal 46% of children are reported anemic study with 27% children mildly anemic, 18% moderately anemic and less than 1%. Found severe anemic¹³. Hemoglobin level below 11.0 gram was considered low¹⁵.

Lower respiratory tract infection being leading cause of death in children less than 5 years of age in developing countries. One study was conducted by KM, Roma Et al 2015 to prove that Anemia can be a risk factor for lower respiratory tract infection. Anemic group was mainly below 2 years of age¹⁴. As in our study the mean age of anemic children was almost 2.5 years.

No significant difference between both gender¹⁴. As is seen

in our study too, no significant difference between gender of children. These findings of our study are comparable with the study conducted by Malla et al (2010)⁸ and Sheikh et al (2014)⁹.

Yanamandala HV et al showed male preponderance 59.1% in control group and 57.3% in study group¹⁶. Maximum number of children in their study were between 3 to 23 months both in study group (80.9%) and control group (81.8%). Age of anemic children in their study was less than reported by our study. Another study showed mean hemoglobin level was 11.6gm/dl in control group and 8.8gm/dl in study group whereas Mean hemoglobin level in our study was 10.83gm/dl in cases and 11.70gm/dl in control group. The Hb level among cases in our study was different to the one reported by Yanamandala et al while among controls it was quite similar. This age group is commonly affected by inadequacy and inappropriate complementary and supplementary feed⁹.

In our study patients found with usual clinical presentation of LRTI, similar clinical presentation was found in the study conducted by Malla et al (2010)⁸. KM et al¹⁴ reported 106 out of 200 children (53%) with hemoglobin level below 11 g whereas in our study there are 38 out of 100 (38%) children were reported with anemia, this percentage is less as compared to above mentioned study.

Another study reported 72% cases of LRTI and 34% non-LRTI controls while in our study 50(50%) of the children were having LRTI and 50(50%) were non-LRTI¹⁷. These finding were consistent with studies conducted by Malla et al⁸ and Sheikh et al (2014)⁹.

As compare to other studies done on Anemia and lower respiratory tract infection, Ramakrishnan et al reported 33% control and 74% cases were Anemic in their study with 200 children and infants between 9 months to 16 years of age¹⁸. Percentage of Anemic children in our study were found significantly higher as compared to the Mourad et al⁷ indicating high prevalence of Anemia in Pakistan. Another study revealed mean serum iron level was found 36ug/dl in anemic patients and 71ug/dl in patients with normal Hb levels having LRTI (P value < 0.01). Studies show that patients with Anemia had 4.99 OR for developing lower respiratory tract infections, while it was 3.2, 5.78 and 2.08, which is showing consistent strength of association of Anemia and acute lower respiratory tract infection. In our studies odds ratio was 4.162 which is similar to the odds ratio reported by above mentioned studies. Only few reports are found in literature review analyzing the role of Low hemoglobin level as a risk factor for developing lower respiratory tract infection. The normal functions of hemoglobin is to facilitates oxygen and carbon dioxide transport. It carries and inactivates nitric oxide and also play role of buffer.⁷ Qualitative and quantitative recession of hemoglobin may adversely affect its normal functions¹⁹. Most probably it may be the cause for low hemoglobin level seen to be as a serious risk factor for developing lower respiratory tract infection as is present in present study where low hemoglobin (Anemic) children were found to be 4.16 times more susceptible to lower respiratory tract infection compared to non-lower respiratory tract infection control group. In one study conducted by Ramakrishnan et al¹⁸ found that anemic children were 5.75 times more susceptible to lower respiratory tract infection, which is more consistent with our study.

Similarly, in one study by Savitha et al²⁰ on modifiable risk factor for lower respiratory tract infections concluded anemia as a significant risk factor. As our study was hospital based and has limitations, the prevalence of exposure and outcome variables may be different in a community setting. This study cannot be conclusive in determining anemia as cause of LRTI alone, as sample size was small.

As per findings of this study a strong association was seen

between anemia and degree of respiratory distress as a manifestation of lower respiratory tract infections.

CONCLUSION

Results of our study showed that children presenting with lower respiratory tract infection possesses significant risk for anemia. Thus, early and accurate diagnosis of anemia in children and treatment of anemia will have a positive effect decreasing pneumonia in children.

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