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Effect of Hemoglobin Level on the Severity of Acute Bronchiolitis in Children: A Case-Control Study

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ABSTRACT

Introduction: Iron deficiency anemia (IDA) is a significant health problem that is seen in about 40% of children worldwide. It affects a child's physical and mental development, performance of work and maintenance of their health. Anemia increases the risk of lower respiratory tract infection in children, yet there is not enough evidence that shows the effect of iron deficiency anemia on acute bronchiolitis.

Aim: To evaluate the effect of anemia on the severity of acute bronchiolitis in infants.

Methodology: A total of 160 infants were included in the study, 100 of whom were having acute bronchiolitis while 60 of them were included as a control group. This contrast analysis was conducted on 3 groups of patients having mild, moderate and severe bronchiolitis. A low haemoglobin level (HB) was below 12 grams/dL. This is considered to be an SD of <2. They ranged from 1 month to 2 years of age.

Results: Children having acute bronchiolitis had comparatively lower haemoglobin level and mean cell haemoglobin concentration (MCHC) than in those who were healthy controls. Whereas, the median red cell distribution was higher in patients with acute bronchiolitis. If patients had a haemoglobin level lower than or equal to 10 grams/dL, it is more likely that thebronchiolitis getting worse, that is increasing ten times in patients with acute bronchiolitis. A negative correlation was seen between the severity of bronchiolitis and haemoglobin level.

Conclusion: Infants suffering from anemia are more likely to have acute bronchiolitis and the intensity of anemia increases the severity of bronchiolitis. In infants, early identification and treatment of iron deficiency anemia may reduce the incidence and severity of acute bronchiolitis.

Key Words: Anemia, Infants, Bronchiolitis, Iron deficiency, Negative correlation, Mean cell haemoglobin concentration

INTRODUCTION

Children are most likely to have acute bronchiolitis in the first 24 months of their life. It is a most common acute lower respiratory tract infection. The main multifactorial agent is the respiratory syncytial virus.[1] In the past few years in Pakistan, hospitalization rates for infants have increased from 0.9% to 4%. It is because of acute bronchiolitis.[2, 3, 4, 5] The severity of bronchiolitis has some risk factors that include age, prematurity, gender or immunodeficiency etc.

Iron deficiency anemia (IDA), is a significant health problem that is seen in about 40% of children worldwide.[6] It affects a child's physical and mental development, performance of work and maintenance of their health. Anemia increases the risk of lower respiratory tract infection in children, yet there is not enough evidence that shows the effect of iron deficiency anemia on acute bronchiolitis.[7-9] This study is conducted to examine whether decreased haemoglobin levels increase the risk of developing acute bronchiolitis in children.

Study design: A case-control study

Place and Duration: This study was conducted at Ghulam Muhammad Mahar Medical College Sukkur Pakistan from August 2020 to August 2021.

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Methodology: A total of 160 children were included in the study, 100 of whom were having acute bronchiolitis and 60 of whom were healthy controls. They ranged from 1 month to 2 years of age. Approval from the local Ethics committee was taken. Children having symptoms of respiratory tract infection, like need of supplemental oxygen and Crepitations or rhonchi, along with nasal obstruction, cough, tachypnea, cyanosis, rhinorrhea, retraction and prolonged expiration were included in the study. [3]

If patients had one or more symptoms, including poor feeding, dehydration or respiratory distress, they were admitted to the hospital. [10] No particular criteria were used to determine whether the diagnosis was bacterial (pneumonia) or viral (bronchiolitis). Instead, the criteria was suggested by the Court to conduct a multi-center research. [11, 12]

The patients were divided into 3 categories of groups having mild, moderate and severe bronchiolitis. They were categorized using Wang respiratory score.[13] The severity of acute bronchiolitis was examined through a clinical scoring system that included respiration and heart rate, general health status and existing chest retractions. These 3 groups of patients had scores ranging from 1-3, 4-8, and 9-12.

The children who were having serious respiratory failure and who had a change in mental status were in need of mechanical ventilation and were quickly transferred to PICU. On the 1st day of admission, some physical examinations and observations were taken. The observations include X-ray, CBC and peripheral blood smear.

Children who were transferred to PICU and those who were born premature, having lung and heart disease, non-respiratory infection, bronchopulmonary dysplasia, immunodeficiency and exposed to passive smoking were excluded from this study.

The healthy control group, who were hospitalized to Paediatric general health center, included those children who were having same age, gender and having no respiratory problem or any other infection.

If the haemoglobin levels were<2 standard deviation, it was diagnosed as anemia.[14] BC 6000 Mindray was used to carry out CBC by flow cytometry. The research's statistical analysis was carried out using IBM SPSS Statistics version 22. Shapiro-Wilk test was used to conduct the normality analysis of the data. Values were indicated as percentages and numbers. There were some variables that were not observed in the normal distribution. These variables were standard deviation and median (ranging from Q1 to Q3). Student's t-test was used to differentiate between these 2 groups, one with normal distribution and the other without normal distribution. Chi-square test was used to compare categorical variables. Kruskal-Wallis Test was done to compare those groups who did not fit the normal distribution. The P-value was considered to be less than 0.05, within a confidence interval of 95 percent. In order to evaluate the cut-off value for haemoglobin level, ROC curve analysis was conducted. A logistic regression test along with risk analysis was conducted to test some factors.

RESULTS

The average age of the children was 5 months and 60 patients were males. In terms of age and gender, no difference could be found between the patient group and control group. Infants having acute bronchiolitis had low median haemoglobin level and low MCHC level. On the other hand, patients with acute bronchiolitis had higher median RDW. The respective data is shown in Table No. 1. When the patients were examined according to the severity of acute bronchiolitis, it was observed that the number of patients in mild, moderate and severe groups were 19, 50 and 21, respectively. Patients with mild acute bronchiolitis had higher haemoglobin levels than the ones having severe acute bronchiolitis. The median value of RDW was 14% in mild, 14.9% in moderate and 15.1% in the severe group. This shows that the severe group had the highest median RDW. Lastly, no difference was found between these groups in terms of MCHC levels. The related data is shown in Table 2.

Table No. 3 shows the values that were evaluated while performing the ROC curve analysis. It shows the haemoglobin cut-off value in the development of severe acute bronchiolitis. Patients having a haemoglobin value less than and equal to 10 grams/dL may be affected with severe bronchiolitis. Table No. 4 shows the risk factors by performing regression analysis. Patients having a haemoglobin level less than and equal to 10 grams/dL had a risk of acute bronchiolitis increasing 10 times. A negative correlation was seen between the severity of acute bronchiolitis and haemoglobin level. However, there was no correlation seen between the severity of acute bronchiolitis and age.

Table 1: Characteristics of the study participants

Variables	Patient group	Control group	P-value
Age (n)	5	5	Not specified
Gender (%)	60 males, 40 females	32 males, 28 females	Not specified
Haemoglobin Level (grams/dL)	10.2	11.2	<0.001
RDW (%)	14.5	14.2	0.032
MCV (fL)	80.2	85.1	Not specified
MCH (pg)	28.4	26.9	Not specified
MCHC (grams/dL)	33.2	34.1	0.012

Table 2: Hemoglobin level, MCHC levels and RDW of the study participants

Variable	Mild	Moderate	Severe	P-value
Haemoglobin Level (grams/dL)	10.2	10.3	9.2	<0.001
MCHC (grams/dL)	33.4	33.7	33.5	0.942
RDW (%)	13.7	14.6	14.9	0.032

Table 3: ROC curve analysis

	Cut-off value	Sensitivity	Specificity	95% confidence interval	P-value
Haemoglobin Level (grams/dL)	≤ 10	0.727	0.823	0.667-0.902	<0.001

Table 4: Risk factors by performing regression analysis

	OR	95% Confidence interval	P-value	Risk
Haemoglobin Level (grams/dL)	10.97	3.125-3.351	<0.001	Yes
Age	0.846	0.301-1.851	0.528	No
Gender	1	0.1997-1.002	0.937	No

DISCUSSION

This research shows that if patients have a haemoglobin level less than or equal to 10 grams/dL, they are more likely to get severe acute bronchiolitis (about 10 times), and these are the patients that remain admitted in the hospital for a longer period of time. This shows a negative correlation between haemoglobin level and severe acute bronchiolitis. Therefore, it is concluded that haemoglobin level is an independent risk factor for the severity of acute bronchiolitis in children.

When haemoglobin level is below a standard deviation of 2, anemia is diagnosed.[15] Countries where the risk of iron deficiency anemia is high, anemia can affect the children with respiratory tract infection up to 60-70 percent.[7,8]

We determined a negative correlation between haemoglobin level and seriousness of acute bronchiolitis. If patients had haemoglobin level ≤ 10 grams/dL, the risk is likely to increase ten times in patients having acute bronchiolitis. Moreover, patients having a haemoglobin level less than 10 grams/dL have a risk of more severe acute bronchiolitis with a sensitivity of 72.7% and specificity of 82.3%. Claimed by Mourad et al., patients with haemoglobin level <11 grams/dL are two times likely to get lower respiratory tract infection than the health control group.[9] As shown by Dhivyanarayani M et al., acute bronchiolitis is the most common cause of lower respiratory tract infection in patients ranged from 2 months to 5 years. The number of days patients were admitted in the hospital were similar in anemic and non-anemic groups. [16] According to Hussain et al., from a group of 220 patients ranged from 1 month to 5 years, anemic patients were 4.6 times more likely to get lower respiratory tract infection. [7] Moreover, according to Malla et al., 150 anemic children ranged from 1 month to 5 years, were 3.2 times more likely to get lower respiratory tract infection. [17]

Iron is a necessary element that impacts the immune system's ability to develop adequate immunity. [18] Some researchers have shown decreased levels of cytokines in iron deficiency anemia. [19] According to Hassan et al., IL-6 levels were low in patients with iron deficiency anemia. A positive correlation was also seen between IL-6 levels and serum iron. [20] Likewise, the same results were seen in the research of Ekiz et al. and Feng-Xue et al. [18,19]

Joynson et al. was the first person to determine the effect of deficiency of iron on the immune system. [20] It was concluded that this deficiency is seen because of decreased cell-mediated immunity, natural killer cell activity and the response of mitogen. The result of low cytokine activity is T-cell dysfunction. T-cell and monocyte cytokines impact the expression of proteins involved in iron uptake and storage, which regulates cellular iron homeostasis. Some cytokines directly produce the duplication and translation of the ferritin. These cytokines include IL-6, IL-1, and TNF-a. Lower IL-6 levels cause the cell-mediated immune mitogen sensitivity and the natural killer activity to decrease. Furthermore, because alveolar macrophages obtain iron predominantly from catabolic erythrocytes and plasma pools, a decrease in haemoglobin level may impair the functioning of normal alveolar macrophages. As a result, in an iron-deficient state, their function may be restricted. [15]

The transport of carbon dioxide and oxygen is eased by haemoglobin. Anemia in acute bronchiolitis determined the fact that excess carbon dioxide cannot be transferred from bypassed areas to the blood with a low haemoglobin level. The principal function of haemoglobin is to carry and deliver

oxygen from lungs to tissues. [14] This excess carbon dioxide will change into dissolved form in the presence of anemia. This would lead to an increase in acute bronchiolitis.

Iron deficiency anemia is most likely to occur in children aged between 3-23 months. [20] In this research, we found out that children less than 2 years with iron deficiency anemia had lower values of MCV and MCHC. Due to the lack of anemia markers, the exact cause of anemia could not be confirmed. Because this test is not available in our setup, the serum ferritin level was not determined, and ferritin levels are unreliable in situations of infection because they rise as an acute phase protein.

CONCLUSION

Overall, it is concluded in this research that the presence of anemia can increase the severity of acute bronchiolitis in infants. To reduce the seriousness of acute bronchiolitis, the treatment of iron deficiency anemia is done in children below 2 years of age.

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