

Original Research Article

Considering lactate dehydrogenase (LDH) concentration in nasal-wash (NW) as a marker in evaluating the outcome of patients with bronchiolitis

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ABSTRACT

Background: Estimation of bronchiolitis severity in infants is still an important issue and there are no standard methods to help physicians for better evaluation and management of clinical status of these patients. The aim of this study was to investigate the role LDH concentration in NW as a biomarker in evaluation the outcome of patients suffering bronchiolitis in Bu Ali Hospital, Ardabil.

Methods: 100 children with bronchiolitis aged below 2 years entered the study. Nasal wash sample was extracted from all patients using 2 ml of normal saline. Samples were sent to laboratory to measure LDH level. Data were analyzed by statistical methods in SPSS.16.

Results: The mean age of patients was 6.9 ± 3.7 months and 57% of them were male. 42% of patients had mild bronchiolitis and 58% of them suffered from severe bronchiolitis. The LDH level of nasal wash fluid was neither related with gender nor with age. But it was significantly lower in patients who required oxygen therapy and had fever compared with those who did not require oxygen therapy and without fever. Moreover, LDH level showed a significant negative association with hospital stay ($r = -0.570$, $p < 0.001$) and bronchiolitis severity ($r = -0.440$, $p < 0.001$) in a way that its concentration was significantly lower in patients with hospital stay longer than 24 hours compared with hospital stay shorter than 24 hours, and in patients with severe bronchiolitis compared with mild bronchiolitis.

Conclusions: According to results of this study, LDH measurement in nasal wash fluid can be used as a biochemical marker to evaluate clinical outcomes of bronchiolitis in children younger than 24 months.

Keywords: Ardabil, Bronchiolitis, Infants, Lactate dehydrogenase

INTRODUCTION

Bronchiolitis is the most common disease of the lower respiratory system in children and the most important causes of hospitalization in this age group which deal to mortality and morbidity in the age group less than two years.¹ Estimating the intensity of the disease in younger infant is still an important problem and there weren't completely accurate standard methods to help doctor to estimate the condition of diseases, therefore, the study

seems to be necessary to find methods based measurable biomarkers to better manage and determine the clinical situation of patients. Recently, several studies have shown that LDH in Nasal-Wash (NW) is a good indicator to determine the intensity of bronchiolitis and this marker can be useful in predicting the intensity of bronchiolitis.²⁻⁶

About 50 to 80 thousand hospitalizations per year attributed to children under one year of age.¹ Respiratory

syncytial virus (RSV) and Rhinovirus were the most common cause of bronchiolitis. The diagnosis of bronchiolitis is a clinical diagnosis and has been done based on patient history and physical examination. Symptoms included fever, cough, wheezing, asthma between ribs retraction, runny nose, crackle, increased pulse and heart rate, decreased oxygen saturation and pulling nose blades with the use of hypodermic muscles.⁷⁻⁹

LDH is an enzyme generally used in routine clinical examination as a marker for cellular damage and inflammation from serum samples. It is expected that in severe illnesses, we will have higher levels of LDH in the nose and rinse as the result of tissue damage the enzyme is released into the extracellular space. However according to recent findings on bronchiolitis which showed that higher levels of LDH in nasal rinse were associated with a lower risk of hospitalization.^{2,3,5}

At present the number of studies conducted in this area is limited in the world and the results of their findings in some countries have been partly contradictory and some studies have shown that there is a reverse and direct relationship between LDH concentration and severity of bronchiolitis. Considering the need for a marker to determine the outcomes of children with bronchiolitis and the limited studies conducted in the world and the lack of a study in Iran, the aim of this study was to investigate LDH in NW as a marker in evaluating the outcome of patients with bronchiolitis in Bu-Ali hospital in Ardabil city, Iran.

METHODS

This cross-sectional study was performed on 100 children under the age of 2 years with a diagnosis of bronchiolitis which hospitalized in Ardabil city Bu-Ali hospital. After receiving written satisfaction, the children were enrolled to the study and in the baseline of all children a sample of NW was prepared by washing with 2cc of normal saline in the nose. After washing the sample was sent to the lab for measuring LDH. Also, the intensity of bronchiolitis determined based on the RDAI score and divided to mild and intense groups.

The scale had 0 to 17 score with score 5 and less considered as the mild bronchiolitis and score 6 and more was considered as the intense bronchiolitis. The method for scoring bronchiolitis based on this scale in Table 1.¹⁰ The LDH concentration and intensity of bronchiolitis in patients with other information including gender, age, fever, need for oxygen therapy, need for intravenous liquid therapy and duration of hospitalization were recorded in a checklist. The inclusion criteria were age less than 2 years, diagnosis of bronchiolitis by pediatrician based on a clinical examination and CXR. Exclusion criteria included cardio pulmonary disease, immunodeficiency, down syndrome, metabolic disease, childhood ventilator, positive family history of asthma and finally childhood illness. For data analysis we used descriptive and analytical methods in SPSS.16.

Table 1: Assessment of bronchiolitis severity in infants based on RDAI scale.¹⁰

Score	Symptoms	0	1	2	3
Wheezing	While exhaling	None	Exhale end	Half an exhale	3 quarters of exhale
	While respire	None	Incomplete	Complete	-
	Number of lobes involved in lung	0	1 or 2	3 or 4	-
Retraction	Supraclavicular	None	Mild	Moderate	Severe
	Between the ribs	None	Mild	Moderate	Severe
	Below the rib cage	None	Mild	Moderate	Severe

RESULTS

Of all infants, 57% were male and rest of them were female. The mean age of children was 6.9 months with a standard deviation of 3.7 month. Most of children was in the age group of 2 to 6 months (48%). 45% of children had fever and 34% need for oxygen therapy. The mean of hospital stay was 3.12 days with a standard deviation of 1.39 days. The mean concentration of LDH in the NW was 336.7±205.34 IU/L it ranged from 111 to 809 IU/L and its median was 291 IU/L. According to RDAI 42% had mild bronchiolitis and 58% had severe bronchiolitis. The mean score of bronchitis severity among children was 6.9±3.8 and there was no significant difference between the two groups of boys and girls in term of LDH concentration in NW. The concentration of LDH in the

NW was correlated with the age of the patients but was not significant. There was no difference between the three age groups of 2 to 6, 6 to 12, and 12 to 24 months in term of concentration of LDH in the NW. The average LDH concentration of NW in the group of patients with fever was significantly lower than patients without fever. The mean concentration of LDH in nasal liquid in patients requiring oxygen therapy was significantly lower than other patients. The concentration of LDH in the NW was significantly inverse correlated with the duration of hospitalization ($r = -0.57$, $P = 0.001$). The concentration of LDH in the NW had significantly negative correlate with their bronchiolitis severity score ($r = -0.44$, $P = 0.001$). The LDH concentration of NW in patients with intense bronchiolitis was significantly less than patients with mild bronchiolitis (Table 2).

Table 2: Relation between LDH concentration and effective variables.

Variables		Mean	SD	P-value
Sex	boy	309.8	194.4	0.13
	girl	379.5	215.2	
Age groups (month)	2-6	365.4	224.6	0.34
	6-12	299.6	185.9	
	12-24	336.8	183.1	
Fever	+	287.8	174.5	0.03
	-	376.8	221.1	
Oxygen therapy	+	209.6	125.5	0.001
	-	402.2	208.4	
Severity of bronchiolitis	mild	434.7	214.8	0.001
	severe	265.8	166.9	

DISCUSSION

The findings of this study showed that the LDH concentration of NW in children low than 24months age had significant relation with severity of bronchiolitis, duration of hospitalization, need for oxygen therapy and the presence of fever in these patients.

Thus, LDH concentration of NW in patients with fever was significantly lower than those without fever ($P=0.30$) and in patients need for oxygen therapy was significantly lower than those who did not need oxygen therapy ($P=0.001$). Also, its concentration had negative correlate with duration of hospitalization ($P=0.001$, $r = -0.570$) and severity of bronchiolitis ($P=0.001$, $r = 0.440$). Also, LDH concentration in patients with intense bronchiolitis was significantly lower than patients with mild bronchiolitis ($P=0.001$).

The findings of this study were in line with the findings of Lahman et al on 101 children aged less than 24months with bronchiolitis which showed that LDH concentration in the NW was significantly reduced the risk of hospitalization.² Also, in line with the findings of this study was the study of Mansbakh and et al on 258 children under the age of 24months with bronchiolitis which showed that higher levels of nasopharyngeal LDH in children with bronchiolitis have a significant relationship with their risk of hospitalization.³

The study of Kanjiano et al on 126 preschool children with bronchiolitis showed that the LDH concentration of NW had inverse relationship with the need for oxygen therapy.⁴ Finding of the study by Mehta et al on children less than 24months old with bronchiolitis in line with our study was found that children with intense bronchiolitis had higher LDH concentration so that children with more intense bronchiolitis who needed to be acceptable to the intensive care unit had significantly higher LDH in the NW than other children.⁵ However the age classification of children in their study showed that LDH concentration of NW had inverse relationship in children between 4 and 12months and had a straight relationship with

hospitalization in children between 12 and 24months which in the present study there wasn't relation between age and LDH concentration. Also, apposite to the findings of this study, the study of Rahman et al in 55 children over 6months of age with bronchiolitis found a straight relationship between the concentration of LDH of NW and the outcomes of bronchiolitis in children.⁵ In their study LDH concentration of NW had a significant positive correlation with the severity of the disease, duration of hospitalization and the duration of oxygen therapy which can be due to fewer newborns and limitation in age up 6months.

The findings of this study also showed that high levels of LDH are associated with better clinical outcomes so that in the present study the occurrence of bronchiolitis had inverse relationship with severity of bronchiolitis, the duration of hospitalization, the need for oxygen therapy and the fever. Studies by Laham et al and Mansbakh et al in the United States showed that LDH concentration in the nasal liquid has a significant inverse relationship with the risk of hospitalization for children under the age of 24month with bronchiolitis.^{2,3} Study by Kanjiano et al in Switzerland showed that LDH concentration in the NW had a reverse relationship with patients need for oxygen therapy.⁴

The study by Mehta et al in the United States showed that LDH concentration in the NW in children aged 4 to 12months has an inverse relationship with the risk of admission but in the 12-24month children with a straight relationship was at risk of being hospitalized.⁵ The study of Rahman et al in Egypt also showed that there was a significant straight relationship between the LDH concentration in NW in children older than 6months with severity of bronchiolitis, duration of hospitalization and oxygen therapy.⁶

CONCLUSION

The findings of this study showed that LDH levels in the NW of children under the age of 24months with bronchiolitis are associated with the outcomes of the disease including the intensity of the disease, the need for oxygen therapy and the presence of fever. The measurement of LDH in NW can be used as a biochemical marker and a fast and cheap test to estimate and evaluate the outcomes of bronchiolitis in these patients. Of course, given that the used of LDH in NW as a marker to specify the outcomes of bronchiolitis is a new issue and studies on this issue currently are few and because of different findings in some studies, further studies are needed to allow LDH to be used for daily use in clinical decision making.

In this study a single sample of nose bleed was taken from each patient at the hospital and preparation of several samples during the hospitalization of patients by changing the course of their disease may be helpful in interpreting the findings.

Another limitation of this study was the lack of measurement of serum LDH levels in patients which study its association with LDH levels in NW can also be helpful in interpreting the finding.

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