

# LACTATE DEHYDROGENASE LEVEL IN BRONCHIAL ALVEOLAR LAVAGE FLUID OF PATIENTS WITH BACTERIAL PNEUMONIA AND TUBERCULOSIS

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**ABSTRACT :** The cytoplasmic enzyme lactate dehydrogenase (LDH), can be found extracellularly in BALF in the presence of lung tissue damage. This study aimed to investigate the level of LDH in the BALF of patient with bacterial pneumonia. A total of 364 patients aged 15-55 years suffering from pneumonia, who underwent bronchoscopy with bronchoalveolar lavage in the International Private Hospital, Baghdad during the period from January 2014 until June 2017 were enrolled in this study. The majority of patients (69.2%) were aged 36 to 55 years. *Streptococcus pneumoniae* accounted for 30.4% of pneumonia cases included in this study, while *Klebsiella pneumoniae*, *Mycobacterium tuberculosis* and *Haemophilus influenzae* accounted for 18.6%, 23% and 28% of cases, respectively. Out of the 364 patients included in this study, 228 (62.6%) had increased levels of LDH in their BALF. Interestingly, patients who were diagnosed with either *Streptococcus pneumoniae* or *Mycobacterium tuberculosis* showed a highly significant increase in LDH levels when compared to patients with normal LDH levels.

**Key words :** Lactate dehydrogenase, BALF, bacterial pneumonia, tuberculosis.

## INTRODUCTION

Lactate dehydrogenase (LDH) is an enzyme responsible for transferring hydrogen and catalysing the oxidation of L-lactate to pyruvate with nicotinamide-adenine dinucleotide (NAD)<sup>+</sup>, as a hydrogen acceptor. Activity of LDH has been described in liver, lungs, brain, kidney, skeletal muscles, lymph nodes, spleen and myocardium, erythrocytes, platelets and leucocytes (Drent *et al*, 1996). It has been reported that pulmonary injury results in elevated tissue levels of LDH which remains high for 3 weeks. The presence of LDH in many organs makes it difficult to pin down the actual cause for any abnormal serum levels of LDH. On the other hand, measurement of total LDH levels in bronchoalveolar lavage fluid (BALF) seems an attractive approach to assess the degree of pulmonary/lung cell injury (Ulloa-Gutierrez, 2008a). Previous studies have described LDH as a useful marker for analysis of patients with complicated pneumonia. This enzyme is a marker of cellular damage and can subsequently be released from cells undergoing primary or secondary necrosis (Rydell-Tormanen *et al*, 2006; Liu *et al*, 2018).

## MATERIALS AND METHODS

Bronchoalveolar lavage fluid was collected from 364 patients aged 15-55 years old suffering from bacterial pneumonia whom underwent bronchoscopy during the

period from January 2014 until June 2017. All BALF samples were collected from the International private hospital in Baghdad. BALF samples were sent for cytological examination, bacteriological analyses to diagnose the causative agent and LDH measurement. The causative agent of pneumonia was detected by Gram staining, cultures, biochemical tests. Bacteriological analyses included gram stain, acid fast stain, culture on blood, chocolate and macConkey agars. After isolation of bacteria from BALF, further investigations were carried out to diagnose the causative agent of pneumonia. Due to the presence of LDH in many organs, LDH serum levels were not investigated. A colorimetric based assay (LDH LR liquid reagent-Gesan, Italy) was used for the measurement of LDH in BALF. LDH levels less than 480 U/L were considered normal, while LDH levels of 480 U/L or more were considered as an increase in this enzyme (Kim *et al*, 2014).

## RESULTS

Distribution of patients according to age revealed that the majority (69.2%) of patients were in the age group 36-55. On the other hand, only 30.8% of patients were aged 15 to 35 years as shown in Fig. 1. These results show that the percentage of patients increase with increased age.

The results of bacterial analyses revealed that 30.4%,

**Table 1** : Percentage of patients with increased and normal LDH levels in BALF of each group.

Causative agent	% of patients with increased LDH levels in BALF	% of patients with normal LDH levels in BALF	P – value increased vs normal LDH
<i>K. pneumoniae</i>	44.1	55.9	NS (P>0.05)
<i>S. pneumoniae</i>	94.5	5.5	HS (P<0.001)
<i>M. tuberculosis</i>	89	11	S(P<0.05)
<i>H. influenzae</i>	19.4	80.6	NS (P>0.05)

S = Significant, NS = Non significant, HS = Highly significant.

18.6%, 23% and 28% of patients had an infection with *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Mycobacterium tuberculosis* and *Haemophilus influenzae*, respectively (Fig. 2).

Measurement of LDH levels in BALF of patients with pneumonia showed that most patients, who were diagnosed with *Streptococcus pneumoniae* as a causative agent of pneumonia (*Pneumococcal pneumonia*), or tuberculosis had increased levels of LDH in their BALF (Fig. 3). Statistical analysis using unpaired T test showed a significant increase (P>0.001) in the percentage of patients with pneumococcal pneumonia and increased levels of LDH in BALF when compared with those with pneumococcal pneumonia and normal levels of LDH. Similarly, there was a highly significant increase in the number of tuberculosis patients with increase LDH levels in BALF when compared to those with normal LDH levels (Table 1).

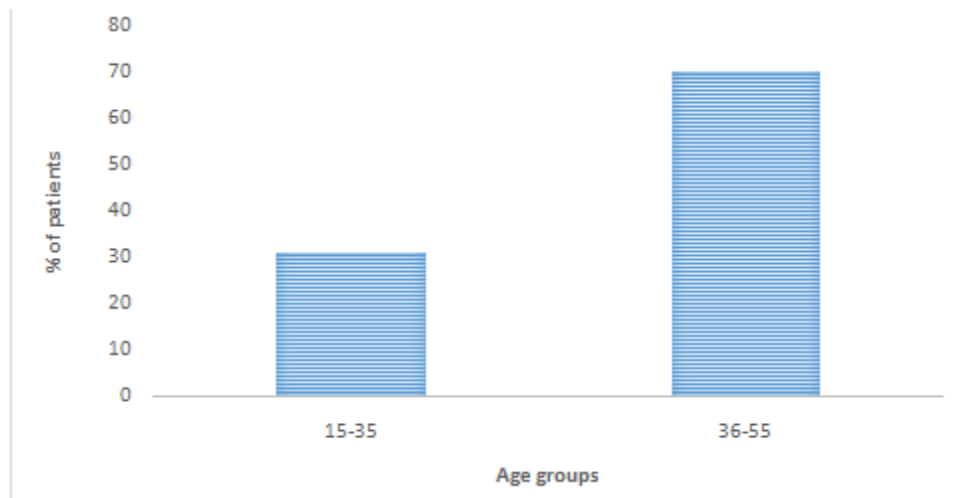
## DISCUSSION

Community acquired pneumonia remains an important health problem especially in developing countries. Several studies have demonstrated the clinical and economical impact of pneumonia in both developed countries (such as the United Kingdom and the United States of America) and developing countries (Welte *et al*, 2012). Data presented in this study has shown that the majority of patients were more than 35 years old confirming that the incidence of pneumonia increases with age. Previous studies have described pneumonia as a disease of the elderly (Welte, 2011).

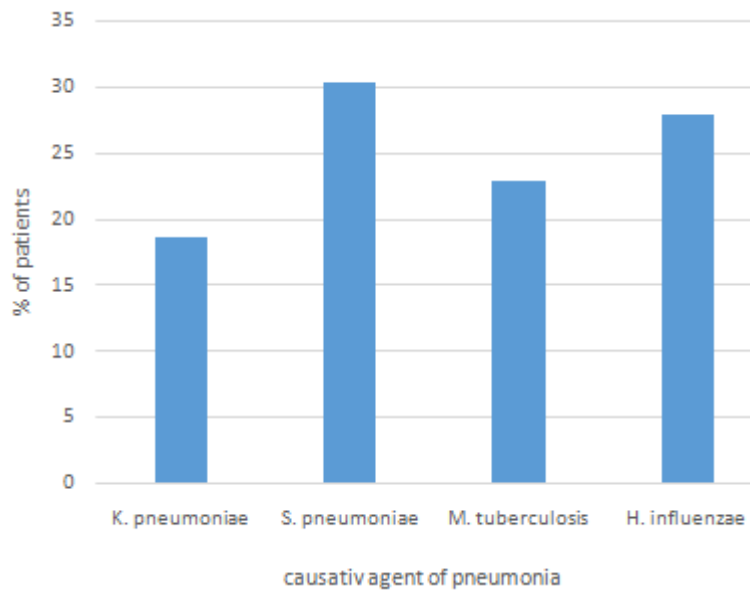
The results of this study also showed that *Streptococcus pneumoniae* remains the most common bacterial etiological agent of pneumonia. *Streptococcus pneumoniae* has been reported in several studies to be the most frequently isolated pathogen in patients with pneumonia. Among the countries, which have reported that streptococcus pneumoniae is the most common cause of community acquired pneumonia in the United States, Europe and Iraq (Lode, 2007; Bartlett and Mundy, 1995; Al-Ghizawi *et al*, 2007). Other pathogens frequently isolated from patients with pneumonia include

*Haemophilus influenzae*, *Klebsiella pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Chlamydia pneumoniae*, *Coxiella burnetii* (Torres *et al*, 2014). Lactate dehydrogenase (LDH) is an enzyme localized in the cytoplasm of cells, capable of converting pyruvic acid to lactic acid during the process of glycolysis. Any loss of membrane integrity results in the release of LDH from cells and subsequently to an increase in the levels of this enzyme. LDH levels reflects cellular damage and indicates that cells are undergoing primary or secondary necrosis (Rydell-Tormanen *et al*, 2006). Hence, measurement of LDH levels can be a useful parameter in both BALF and pleural fluid analysis for patients with pneumonia (Petruševska Marinković *et al*, 2011; Wu *et al*, 2017). Measurement of LDH in BALF of patients diagnosed with either *Streptococcus pneumoniae* or *Mycobacterium tuberculosis* in this study showed that the majority of patients (94.5 and 89%, respectively) had increased levels of LDH. These results are in agreement with Ulloa-Gutierrez who has previously reported very high LDH levels in specimens obtained from patients diagnosed with pneumococcal pneumonia. Furthermore, it has been demonstrated that the severe pulmonary inflammation during some bacterial pneumonia results in apoptotic neutrophils undergoing secondary necrosis. These apoptotic neutrophils are thought to be the primary source for LDH in bronchoalveolar lavage fluid (Ulloa-Gutierrez, 2008b). The increase of LDH in BALF of patients with tuberculosis has previously been reported. The increase in LDH in BALF have also been proposed as a useful marker to differentiate active pulmonary tuberculosis from inactive pulmonary tuberculosis. It has been suggested that low (less than 24 mIU/L) LDH levels in BALF is indicative of inactive pulmonary tuberculosis (Emad and Rezaian, 1999; Alavi *et al*, 2008; Al Shammari *et al*, 2015). Caseous necrosis is the pathophysiological hallmark of tuberculosis (O'Garra *et al*, 2013) and thus would explain the increase in the number of tuberculosis patients, who had increased levels of LDH in their BALF.

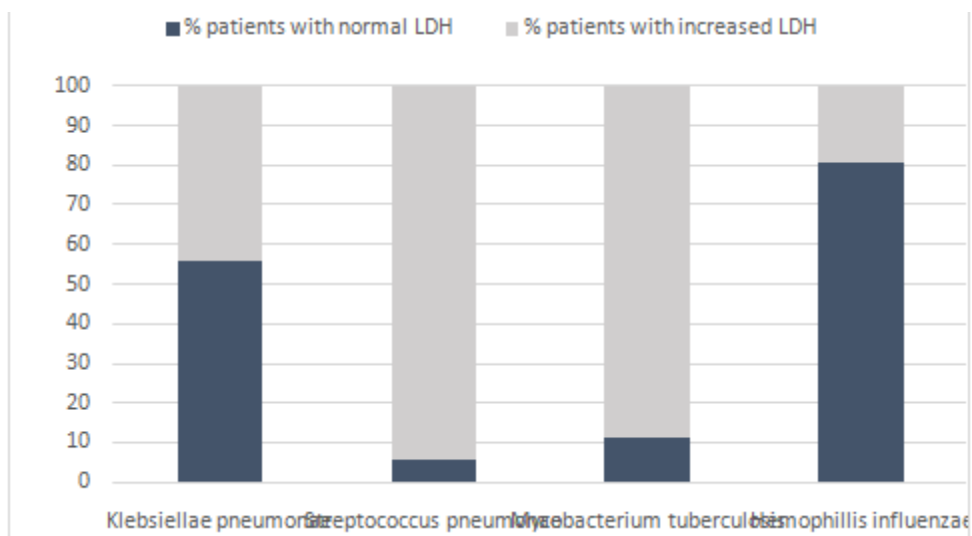
Among patients diagnosed with *Klebsiella pneumoniae*, no significant difference was found between



**Fig. 1 :** Distribution of patients according to age groups.



**Fig. 2 :** Distribution of patients included in the study according to the causative agent of pneumonia.



**Fig. 3 :** Distribution of patients according to causative agent and LDH levels (normal or increased) in BALF.

patients with normal BALF LDH and those with increased levels of LDH. Most of patients diagnosed with *Haemophilus influenzae* had normal levels of LDH in BALF, probably indicating that tissue damage is minimal in those patients. In addition, tissue necrosis as a result of these two microorganisms mostly occur in immune compromised patients (Paczosa and Meccas, 2016).

### CONCLUSION

Elevated LDH levels in BALF can be used as an indicator of the severity of cellular damage in patients suffering from pneumonia and the degree of cellular necrosis in tuberculosis patients.

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