*RADS-JPPS Vol 4 (1), June 2016, 123-127*

# The Relationship Between the Serum High-Mobility Group Protein B1 (HMGB1) Level with the Severity of the Patient's Condition in Different Severe Pneumonia Patients Complicated with Acute Respiratory Distress Syndrome (ARDS)

*Yanqiu Gao[1*], Min Liu[2], Hua Zhang[1]*

[1]Respiratory Intensive Care Unit, Zhengzhou Central Hospital Affiliated to Zhengzhou University, Zhengzhou city, PR China

[2]Cardiovascular internal medicine, Zhengzhou Central Hospital Affiliated to Zhengzhou University, Zhengzhou city, PR China

## ABSTRACT

**Objective To observe the serum high-mobility group protein B1( HMGB1) level in severe pneumonia patients complicated with acute respiratory distress syndrome( ARDS) and explore its relation to the severity of the patient's condition. Methods Thirty-six severe pneumonia patients complicated with ARDS received mechanical ventilation in ICU between 2012 and 2014 were selected, and the patients were divided into survival group( n= 21) and death group (n= 15)according to prognosis. At 1- and 3-day and the day of discharge from ICU or death, serum HMGB1 level was detected by enzyme-linked immunosorbent assay( ELISA) ,and the Acute Physiology and Chronic Health Evaluation II( APACHE II) score was made. Sixteen healthy subjects for physical examination in the same time were selected as control group. Results:At 1- and 3-day and the day of the death, serum HMGB1 level and APACHE II scores presented increase tendency( all P<0.01) in death group and they presented decrease tendency at day 1-,3-day and the day of discharge from ICU(all P<0.01) in survival group. The serum HMGB1 levels of three time-points decreased in the order of death group, survival group and control group (all P<0.01). APACHE II scores of three-points in death group were all significantly higher than those in survival group (all P<0.01). Serum HMGB1 levels were positively correlated with the APACHE scores ( r =0. 691,P<0.01) . ConclusionSerum HMGB1 level in severe pneumonia patients complicated with ARDS is positively correlated with the disease severity, and thereby it can serve a clinical index to assist evaluating disease condition and judging prognosis.**

***Keywords:*** *High-mobility group protein B1; Severe pneumonia; Acute respiratory distress syndrome; Acute Physiology and Chronic Health Evaluation II score*

## INTRODUCTION

Acute respiratory distress syndrome was a serious stage of acute lung injury which was mainly caused by severe pneumonia[1]. The clinical features of ARDS were respiratory distress, refractory hypoxemia and non-cardiogenic pulmonary edema[2]. Although the prognosis has improved in recent years, but the severe pneumonia complicated with ARDS was still a dangerous illness characterized by rapid development and higher mortality. Sepsis is the main pathological mechanism of ARDS[3, 4]. High-mobility group protein B1 is an important inflammatory mediators secreted by immune cells and then released into the extracellular or peripheral circulation[5]. It was mainly involved in septic arthritis and other inflammatory reactions, but the relationship between HMGB1 and severe pneumonia

complicated by ARDS was rarely reported. In this study, we observed the serum high-mobility group protein B1( HMGB1) level in severe pneumonia patients complicated with ARDS and explore its relation to the severity of the patient's condition. The results were as follows.

## MATERIALS AND METHODS

### *Clinical materials*

Thirty-six severe pneumonia patients complicated with ARDS received mechanical ventilation in ICU between 2012 and 2014 were selected, and the patients were divided into survival group ( n= 21) and death group( n= 15) according to prognosis. In the survival group, there were male (12 cases), female(9 cases); the age was between 26 and 73. In the survival group, there were male (8 cases), female(7 cases); the age was between 24 and 71. Sixteen healthy subjects for physical examination in the same time were selected as control group. Among them, there were male (8 cases), female(8 cases) and the age was between 25 and 70.

### *Diagnostic criteria*

The diagnostic criteria for ARDS were supported by the Chinese Medical Association of Critical Care Medicine in 2006[6]. The 36 patients in the observation group were all meet with the the diagnostic criteria of severe pneumonia.

### *Observed indicator*

The general information including temperature, leukocyte count, arterial blood gas, oxygenation index was recorded for the severe pneumonia complicated by ARDS patients. At 1- and 3-day and the day of discharge from ICU or death, the Acute Physiology and Chronic Health Evaluation II score was made. Meanwhile, the blood samples were collected. Then the serum was separated and stored at -80 until analysis. The blood samples and serum of healthy subjects were also processed according to the above conditions. Serum HMGB1 concentrations were measured by HMGB1 enzyme-linked immunosorbent assay kit(Japan, SHINO-TEST company).

### *Statistical analysis*

All data were assessed by SPSS 21.0 program. The quantitative data was represented by (x±S). HMGB1 concentration in serum and APACHE score were compared by variance analysis of repeated measures in groups; The single factor analysis of variance was performed among groups. Correlation between serum HMGB1 concentration and APACHE score was analyzed by Pearson correlation analysis. Differences were considered to be statistically significant at $P< 0.05$.

## RESULTS

### *The results of serum HMGB1 concentration*

At 1- and 3-day and the day of the death, there was an increase tendency( all $p<0.01$)

**Table 1:** The levels of serum HMGB1 in death, survival and control group ( ng /ml, x±s)

| Group | Cases | 1d | 3d | transferred from other departments or death | F value | P value |
|---|---|---|---|---|---|---|
| Death group | 15 | 15.40 ± 1.80 | 16.80 ± 1.52 | 21.40 ± 2.06 | 45.113 | <0.01 |
| Survival group | 21 | 8.10± 1.18 | 6.86± 1.24 | 3.48 ± 1.21 | 82.201 | <0.01 |
| Control group | 16 | 1.93± 0.28 | 1.93± 0.28 | 1.93 ± 0.28 | | |
| F value | | 461.981 | 678.549 | 1010.278 | | |
| P value | | < 0.01 | < 0.01 | <0 .01 | | |

**Table 2:** The APACHE II scores in death group and survival group(x±s)

| Group | Cases | 1d | 3d | transferred from other departments or death | F value | P value |
|---|---|---|---|---|---|---|
| Death group | 15 | 61.87± 2.03 | 63.33± 1.50 | 97.93± 6.45 | 390.643 | <0.01 |
| Survival group | 21 | 53.24± 2.49 | 44.52± 3.16 | 30.24± 1.89 | 430.268 | <0.01 |
| F value | | 11.046 | 21.366 | 45.632 | | |
| P value | | <0.01 | <0.01 | <0.01 | | |

in death group for the serum HMGB1 level . However,they presented decrease tendency at day 1-3-day and the day of discharge from ICU(all p<0.01) in survival group. The serum HMGB1 levels of three time-points decreased in the order of death group,survival group and control group(all p<0.01). The difference was statistically significant (p<0.01). The data was shown in Table 1.

***The APACHE II scores of severe pneumonia patients complicated with ARDS***

At 1 and 3-day and the day of the death, there was an increase tendency (all P < 0.01) in death group for APACHE II scores of severe pneumonia patients complicated with ARDS. However, they presented decrease tendency at day 1-,3-day and the day of discharge from ICU(all P<0.01) in survival group. The APACHE score in the death group was higher than that in the survival group at thirteenth days and the day of death. The data was shown in Table 2.

***Correlation between serum HMGB1 concentration and APACHE score***

Pearson correlation analysis showed that serum HMGB1 level and APACHE score in patients with severe pneumonia complicated with ARDS were positively correlated (r = 0.691, p < 0.01).

## DISCUSSION

At present, it was considered that the mechanism of severe pneumonia complicated with ARDS was related to the immune factors which could lead to the damage of endothelial cells in alveolar epithelium and then resulted in diffuse pulmonary interstitial and alveolar edema [7, 8]. The study reported that sepsis was the main pathological mechanism of ARDS. It was believed that inflammatory response plays an important role in the prognosis of severe pneumonia, and HMGB1 was one of the hot spots in sepsis [9, 10]. Different from other classic cytokines, HMGB1 belonged to an inflammatory medium of advanced stage. It would rise to peak concentration after the general incidence of 24 h and the duration was long. HMGB1 was secreted by activated immune cells, such as macrophages, monocytes, mature dendritic cells and natural killer cells[11]. It could act on immune cells and endothelial cell surface receptors, which promote the release of a variety of cytokines, adhesion molecules and chemokines[12]. It caused tissue damage by destructing epithelial barrier chemokine inflammatory cells and amplifying the inflammatory response[13]. The previous study show that the level of HMGB1 was closely relatedly to the severity and mortality of sepsis. In addition, there were also study reported that HMGB1 was associated with acute lung injury, pulmonary

fiber[14], and shock. In recent years, many studies have focused on the clinical application of extracellular HMGB1 levels, but the studies about the changes of serum HMGB1levels in patients with severe pneumonia complicated with ARDS and the relationship between the prognosis and HMGB1 levels were rare.

In this study, the results showed that there was an increase tendency in death group for APACHE II scores of severe pneumonia patients complicated with ARDS at 1- and 3-day and the day of the death. However, they presented decrease tendency at day 1-,3-day and the day of discharge from ICU in survival group. The serum levels of HMGB1 in the three time points for death group were significantly higher than that in the control group and survival group, and the difference was statistically significant. The results revealed that the level of serum HMGB1 in the death group increased with the deterioration of the disease and it decreased with the improvement of the disease. In conclusion, the concentration of serum HMGB1 was consistent with the degree of disease which was consistent with the results of Tseng et al [15].

Clinical APACHE scoring system was widely used in the prediction of prognosis of critically ill patients [12]. The higher APACHE II score patients got, the worse the prognosis and higher mortality rate patients had[16]. Pearson correlation analysis showed that serum HMGB1 concentration in patients with severe pneumonia complicated with ARDS was positively correlated with APACHE score.

To sum up, serum HMGB1 concentration in patients with severe pneumonia complicated with ARDS could reflect the extent of the disease and it could be used as a clinical index of severity to assess prognosis.

## REFERENCES

1. Lamontagne F, Briel M, Guyatt GH, Cook DJ, Bhatnagar N, Meade M. Corticosteroid therapy for acute lung injury, acute respiratory distress syndrome, and severe pneumonia: a meta-analysis of randomized controlled trials. Journal of critical care. 2010, 25(3):420-35.
2. Chang DW, Huynh R, Sandoval E, Han N, Coil CJ, Spellberg BJ. Volume of fluids administered during resuscitation for severe sepsis and septic shock and the development of the acute respiratory distress syndrome. Journal of critical care. 2014, 29(6):1011-5.
3. Afshar M, Smith GS, Cooper RS, Murthi S, Netzer G. Trauma Indices for Prediction of Acute Respiratory Distress Syndrome. Journal of Surgical Research. 2015.
4. Chawla R, Mansuriya J, Modi N, et al. Acute respiratory distress syndrome: Predictors of noninvasive ventilation failure and intensive care unit mortality in clinical practice. Journal of critical care. 2015.
5. Chen S-W, Chang C-H, Chu P-H, et al. Risk factor analysis of postoperative acute respiratory distress syndrome in valvular heart surgery. Journal of critical care. 2015.
6. Zhao W, Ge X, Sun K, et al. Acute respiratory distress syndrome after orthotopic liver transplantation. Journal of critical care. 2015.
7. Bhargava M, Becker TL, Viken KJ, et al. Proteomic profiles in acute respiratory distress syndrome differentiates survivors from non-survivors. PloS one. 2014, 9(10):e1097-13.
8. Zhou H, Ji X, Wu Y, et al. A dual-role of Gu-4 in suppressing HMGB1 secretion and blocking HMGB1 pro-inflammatory activity during inflammation. PloS one. 2014, 9(3): e896-34.
9. Standiford TJ, Ward PA. Therapeutic targeting of acute lung injury and acute respiratory distress syndrome. Translational research : the journal of laboratory and

clinical medicine. 2015.

10. Argyriou G, Vrettou CS, Filippatos G, Sainis G, Nanas S, Routsi C. Comparative evaluation of Acute Physiology and Chronic Health Evaluation II and Sequential Organ Failure Assessment scoring systems in patients admitted to the cardiac intensive care unit. Journal of critical care. 2015, 30 (4):752-7.
11. Kassim M, Yusoff KM, Ong G, Sekaran S, Yusof MY, Mansor M. Gelam honey inhibits lipopolysaccharide-induced endotoxemia in rats through the induction of heme oxygenase-1 and the inhibition of cytokines, nitric oxide, and high-mobility group protein B1. Fitoterapia. 2012, 83 (6):1054-9.
12. Fadaizadeh L, Tamadon R, Saeedfar K, Jamaati HR. Performance assessment of Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology Score II in a referral respiratory intensive care unit in Iran. Acta anaesthesiologica Taiwanica : official journal of the Taiwan Society of Anesthesiologists. 2012, 50 (2):59-62.
13. Brinkman S, Bakhshi-Raiez F, Abu-Hanna A, et al. External validation of Acute Physiology and Chronic Health Evaluation IV in Dutch intensive care units and comparison with Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology Score II. Journal of critical care. 2011, 26 (1):105 e11-8.
14. Entezari M, Javdan M, Antoine DJ, et al. Inhibition of extracellular HMGB1 attenuates hyperoxia-induced inflammatory acute lung injury. Redox biology. 2014, 2:314-22.
15. Tseng CC, Fang WF, Leung SY, et al. Impact of serum biomarkers and clinical factors on intensive care unit mortality and 6-month outcome in relatively healthy patients with severe pneumonia and acute respiratory distress syndrome. Disease markers. 2014, 2014, 804654.
16. Keegan MT, Harrison BA, Brown DR, Whalen FX, Cassivi SD, Afessa B. The acute physiology and chronic health evaluation III outcome prediction in patients admitted to the intensive care unit after pneumonectomy. Journal of cardiothoracic and vascular anesthesia. 2007, 21(6):832-7.