

# Serum Albumin Level as A Predictor of Mortality in Patients with Ventilator-associated Pneumonia

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## ABSTRACT

**Background:** Ventilator-associated pneumonia (VAP) is considered as the most common nosocomial infection in the intensive care unit (ICU) with high mortality rates. Hypoalbuminemia has been recognized as poor prognostic indicator in critically ill patients but its role in patients with VAP is not fully known. The aim of this study was to evaluate the role of initial serum albumin in predicting the mortality of patient with VAP.

**Method:** We designed a retrospective study to analyze data from hospitalized patients with VAP between 2003 – 2012 in Cipto Mangunkusumo Hospital, a tertiary hospital in Indonesia. Patients were grouped based on their initial serum albumin levels into: Group-1 (less than 2.7 g/dL), Group-2 (2.7 to 3.5 g/dL), and Group-3 (above 3.5 g/dL). We analyzed the hazard of in-hospital-mortality with cox proportional hazard model.

**Results:** Out of 194 patients evaluated in this study, 95 patients (49%) were included in Group-1, 83 patients (42.8%) in Group-2, and 16 patients (8.2%) in Group-3. Overall mortality rate was 58.2%. The hazards of in-hospital-mortality in Group-1 and Group-2 were 2.48 (95% CI 1.07 to 5.74;  $p = 0.033$ ) and 1.42 (95% CI 0.60 to 3.34;  $p = 0.43$ ), respectively, compared to Group-3.

**Conclusion:** Hypoalbuminemia increases the risk of mortality and initial serum albumin level should be considered as a predictor of mortality in every patient with VAP.

**Key words:** Serum albumin, predictor, mortality, VAP.

## ABSTRAK

**Latar Belakang:** Ventilator-associated pneumonia (VAP) merupakan infeksi nosokomial yang paling sering ditemukan di *intensive care unit* (ICU) dan memiliki angka mortalitas yang tinggi. Hipoalbuminemia telah lama diketahui sebagai petanda prognosis buruk pada pasien dengan penyakit kritis, namun peranannya pada pasien VAP belum jelas diketahui. Penelitian ini bertujuan untuk mengetahui peranan albumin serum inisial dalam memprediksi mortalitas pasien VAP.

**Metode:** Kami melakukan penelitian kohort retrospektif dengan menganalisis data pasien VAP yang dirawat di Rumah Sakit Cipto Mangunkusumo selama kurun waktu tahun 2003 – 2012. Pasien dibagi menjadi tiga kelompok berdasarkan kadar albumin serum inisial: Grup-1 (kurang dari 2,7 g/dL), Grup-2 (2,7–3,5 g/dL), dan Grup-3 (lebih dari 3,5 g/dL). Risiko mortalitas selama perawatan dianalisis dengan *Cox proportional hazard model*.

**Hasil:** Dari 194 pasien yang diikutsertakan, sebanyak 95 (49%) pasien termasuk dalam Grup-1, 83 (42,8%) pasien termasuk dalam Grup-2, dan 16 (8,2%) pasien termasuk dalam Grup-3. Mortalitas selama perawatan terjadi pada 58,2% subjek. Rasio hazard terjadinya mortalitas untuk Grup-1 dan Grup-2 adalah 2,48 (IK 95% 1,07 sampai 5,74;  $p = 0,033$ ) dan 1,42 (IK 95% 0,60 sampai 3,34;  $p = 0,43$ ) apabila dibandingkan dengan Grup-3.

**Simpulan:** Adanya hipoalbuminemia akan meningkatkan risiko mortalitas. Kadar albumin serum inisial sebaiknya dipertimbangkan sebagai prediktor mortalitas pada pasien VAP.

**Kata kunci:** albumin, prediktor, mortalitas, VAP.

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## INTRODUCTION

*Ventilator-associated pneumonia* (VAP) is pneumonia that develops 48–72 hours after the use of mechanical ventilation.<sup>1</sup> Rumende (2008) reported the incidence of VAP at Cipto Mangunkusumo Hospital, Jakarta (RSCM) by 36% with a mortality rate of 51.4%.<sup>2</sup> It is very important for every physician to understand the predictors of mortality as to facilitate clinical decision-making and the basis for education to patients and families. Until now, studies on predictors of mortality of VAP still show various results.<sup>3–5</sup>

Albumin is a serum protein that plays a role in maintaining intravascular oncotic pressure and transporting various molecules including drugs. Hypoalbuminemia is often found in acute or chronic medical condition. In addition to become a risk factor, hypo-albuminemia is also studied as one of the predictors of mortality in patients treated in ICU.<sup>6,7</sup> Pinheiro found that hypoalbuminemia is one independent predictor of mortality in ICU patients with *Pseudomonas* infection.<sup>8</sup> However, the role of serum albumin predicting mortality in ICU patients with VAP is still unclear.

This study aimed to determine the role of serum albumin in predicting mortality initials VAP patients.

## METHODS

This study is a prognostic study with a retrospective cohort design. The author conducted data analysis of VAP adult patients (aged 18 years or older) who were treated at RSCM during time period 2003 to 2012. Subjects were selected consecutively. Data collected included demographic data, clinical, and initial serum albumin level at the time VAP diagnosis was made. Patients were grouped into three groups based upon their initial serum albumin levels, ie Group-1 (albumin less than 2.7 g/dL), Group-2 (albumin 2.7 to 3.5 g/dL), and Group-3 (albumin more than 3.5 g/dL). Outcomes assessed were the condition of the patient at discharge from hospital, alive or dead.

The data obtained from medical records were then converted into variables and analyzed using SPSS version 17.0. Categorical data were presented in the form of numbers and percentages. Numerical data with normal distribution were presented as means and standard deviations. Numerical data with not normal distribution were presented as medians and ranges. The

risks of mortality during treatment were analyzed using Cox proportional hazard models. This study has received ethics approval by Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia.

## RESULTS

During the study, 201 VAP patients were obtained. Seven patients were excluded because their data were incomplete. A total of 194 patients met inclusion criteria. Ninety five subjects (49%) were in Group-1, 83 subjects (42.8%) were in Group-2, and 16 subjects (8.2%) were in Group-3. Characteristics of the subjects are presented in Table 1. Mean APACHE II scores obtained on the Group-1 was 15.4 (SD 7.5), Group-2 was 15.4 (SD 6.0), and Group-3 was 13.6 (SD 5.4). There was no significant difference in the mean APACHE II scores between each group ( $p > 0.05$ ).

**Table 1. Subjects' Characteristics**

Characteristics	Alive n = 81	Dead n = 113
Age (year), mean (SD)	42,8 (15,3)	47,5 (17,1)
APACHE II, mean (SD)	12,9 (5,4)	16,9 (7,1)
Male, n (%)	43 (53,1)	61 (54,0)
Early onset, n (%)	40 (49,4)	59 (52,2)
Surgical patients, n (%)	61 (75,3)	73 (64,6)

Mortality during treatment occurred in 58.2% subjects. The mortality hazard ratios of Group-1 and Group-2 were 2.48 (95% CI 1.07 to 5.74;  $p = 0.033$ ) and 1.42 (95% CI 0.60 to 3.34;  $p = 0.43$ ) compared to Group-3. Figure 1 shows the increase in mortality hazard ratio during hospitalization based on initial serum albumin levels.

## DISCUSSION

High mortality rate found in this study is influenced by various factors. Rumende (2008) showed lower mortality rate in ICU probably because of differences in sample sizes (194 vs 35 subjects) and length of the studies (10 vs 2 years).<sup>2</sup>

Huang and Tseng in Taiwan found that the mortality rate was relatively low (50% and 44.8%).<sup>4,5</sup> One of the factors that may explain these differences is less than optimal management of VAP patients in this study. This is based on the difference between initial APACHE II scores of Huang and our studies. Huang reported a higher APACHE II score (23.2 (SD 5.9)), however this study got higher mortality rate.

Another possibility is the use of different treatments and facilities between developed and developing countries. Resende showed mortality in VAP patients was much higher in Brazil (78.8%).<sup>9</sup>

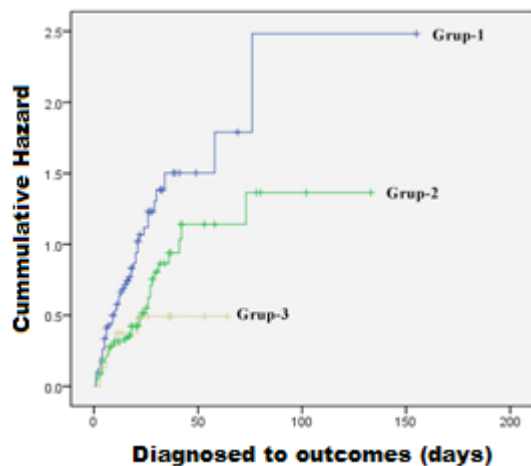


Figure 1. Comparisons among groups

In this study, increase in mortality hazard was in accordance with decrease in serum albumin level. Decreased levels of albumin is proportional to increased mortality risk. Results obtained is in accordance with a meta-analysis conducted by Vincent to critically ill patients in ICU.<sup>6</sup> Although there was no significant difference between Group 2 and Group-3, we found a trend towards an increase in mortality hazard due to decreased levels of serum albumin. This result might be related to albumin level cut-off values used in groups selection. Vincent found that albumin therapy (target = 3.0 g/dL) reduced the risk of complication.<sup>6</sup> This study did not distinguish serum albumin in Group-2 based on therapy targets. However, as shown in Figure 1, the increase in cumulative mortality hazard in Group-2 tends to occur with increased duration of treatment.

Vincent also reported that nutritional status and inflammation did not correlate with hypoalbuminemia and poor outcome.<sup>6</sup> This study did not observe nutritional and inflammatory status of the subjects. APACHE II scores were related to clinical severity. We got no significant differences between the mean APACHE II score of each group. With consideration that serum albumin level is not included in the calculation of APACHE II score, the basic characteristics of the patients at the time of diagnosis can be balanced for comparison.

To the best of our knowledge, there is still no study of hypoalbuminemia as a predictor of mortality in VAP

patients. Bhattacharya found that hypoalbuminemia was not associated with mortality in ICU patients using mechanical ventilators in India.<sup>10</sup> However, big difference in sample sizes, compared to our study, makes Bhattacharya's results should be carefully interpreted.

This is the first study in Indonesia to analyze the relationship hypoalbuminemia and mortality of VAP. Supported by a large sample, this study may represent a population of VAP in ICU patients in major cities of Indonesia.

Nevertheless, retrospective cohort design used has limitations in reflecting the severity of the patient's clinical conditions appropriately.

## CONCLUSION

Hypoalbuminemia increases the risk of mortality. Initial serum albumin level should be considered as a predictor of mortality in patients with VAP.

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