CASE REPORT

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# The C-reactive protein/albumin ratio as a predictor of mortality in sepsis patients in ICU H. Adam Malik Hospital Medan and connected to SOFA score

Taufik Abdi,[1*] Yutu Solihat,[2] Ratna Akbari Ganie[1]

## ABSTRACT

**Background:** Sepsis is a major cause of mortality in the ICU. Therefore, estimating patient mortality from ICU treatment rooms is very important. Organ failure is one of the reasons for the high mortality rates of ICU patients. Accordingly, the study acquires a biomarker that can predict the mortality in which way it can reflect the concept of inflammation from sepsis. This study aims to observe the CRP/Albumin ratio associated with the SOFA score to predict mortality in septic patients.

**Methods:** This study took the blood samples of 58 patients who were being treated at the ICU. Samples were checked for CRP and Albumin on day 1 and 3. At the same time, the SOFA scores and CRP/Albumin ratios were also calculated on day 1 and 3. Finally, the study was conducted after obtaining ethical approval and informed consent.

**Result:** 30 men (51.7%) and 28 women (48.3%) with the youngest was 16 years old, and the oldest was 65. The 1st day of CRP/Albumin ratio did not have a significant relationship with day 1 of the SOFA scores ($p>0.05$) and so does not for the 3rd day that has a significant association with day 3 of the SOFA scores ($p<0.05$).

**Conclusion:** The CRP/Albumin ratio and SOFA score could predict the mortality of septic patients.

**Keywords:** Sepsis, CRP/Albumin ratio, SOFA score

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[1]Clinical Pathology Department, Faculty of Medicine, University of Sumatera Utara/H. Adam Malik Hospital, Medan, Indonesia
[2]Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, University of North Sumatra/ H. Adam Malik Hospital, Medan, Indonesia

*Correspondence to: Taufik Abdi; Clinical Pathology Department, Faculty of Medicine, University of Sumatera Utara/H. Adam Malik Hospital, Medan, Indonesia
taufik.abdi@gmail.com

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## INTRODUCTION

Sepsis is a condition that is very common and causes high mortality and health costs. At present, sepsis is still the leading cause of morbidity and mortality in the Intensive Care Unit (ICU). Every year, an estimated 400,000 to 500,000 patients experience sepsis throughout Europe and the United States, and the average cost per individual case is around the US $ 22,000.[1,2]

Organ failure is one of the causes of the high mortality and morbidity of patients in the ICU and the high costs that must be incurred. Therefore, evaluation of organ dysfunction at all times, during treatment at the ICU is critical. According to the Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2016, sepsis is a state of organ dysfunction.[2] Clinically, organ dysfunction has an increase in sequential organ failure assessment (SOFA) scores > 2 points or more related with an increased risk of death at hospital > 10%.[1,2,3]

Data on sepsis cases at the H. Adam Malik central public hospital in Medan, in 2015 were found in 233 cases. While the data obtained from the H. Adam Malik Hospital General Hospital ICU for the period of January-July 2017, the mortality rate of ICU patients was still high. Every month there were 5 - 7 cases of sepsis patients and 2 - 3 patients die after being diagnosed and starting to be treated in ICU.[4,5] Because organ failure is one of the leading causes of mortality in the ICU, the assessment model is developed to describe the level of the severity of the disease in ICU patients or to predict the outcome of intensive care, namely the Sequential Organ Failure Assessment (SOFA).[6]

In addition to using the SOFA score, it also use biomarkers to predict the mortality of septic patients or septic shock; these biomarkers must be able to reflect the concept of inflammation that plays a role in the pathophysiology of sepsis. Biomarkers that can be used to predict mortality in sepsis patients is the ratio of CRP/Albumin.[7,8] C-reactive protein (CRP) is an acute phase protein that significantly increases infection, and the magnitude of the increase correlates with the severity of the infection. Albumin is a negative acute phase protein. The level of hypoalbuminemia in sepsis patients correlates with the intensity of the inflammatory response triggered by the infection.[9,10,13,14] Based on those concepts, the CRP/Albumin ratio can be used as a biomarker predictor of mortality in patients with sepsis or septic shock. And high mortality and poor prognosis are seen in patients with a CRP/Albumin ratio > 2.[7,8]

## METHODS

This study was an observational study with a cohort study design conducted from April to June 2018. The study was conducted in the Clinical Pathology Department of the Faculty of Medicine, University of North Sumatra/H. Adam Malik Hospital in Medan in collaboration with the Department of Anesthesiology and Intensive Therapy at the Faculty of Medicine, University of North Sumatra. The subjects of the study were male and female patients who were admitted to the ICU General Hospital. H. Adam Malik Hospital Medan with the diagnosis of sepsis.

The sample size in this study was determined at 58 samples who met the sepsis criteria according to the Surviving Sepsis Campaign: The International Guidelines for Management of Severe Sepsis and Septic Shock: 2016 which were treated at the ICU H. Adam Malik Hospital Medan, aged > 18 years and < 65 years, and agree to join the study. The exclusion criteria are no therapy that can increase albumin levels and malignancy. In each sample, CRP and albumin were examined on day 1 and 3. The examinations include vital signs like GCS, platelets, total bilirubin, creatinine, blood gas analysis for the assessment of SOFA scores day 1 and 3. CRP examination using serum that was examined using automatic device Ichroma II cell counter analyzer, with the principle of immunoassay examination (ELISA). The examination of albumin using serum was conducted using an automatic cell counter analyzer Architect Plus C1 4100 with the principle of spectrophotometric examination.

## RESULT

Of the thirty people, 51.7% were male, as against 48.3% were women. The youngest age was 16 years, and the oldest was 65 (Table 1).

At the initial measurement, the minimum CRP level was obtained on the first day with a minimum value of 23.37 mg/dl and a maximum of 285.12 mg /dl with a median of 70.63 mg/dl. While the minimum level of CRP on the third day with a minimum value of 25.29 mg/dl and a maximum of 300 mg/dl with a median of 89.60 mg/dl. Minimum levels on the first day albumin with a minimum value of 1.3 g/dl and a maximum of 3.8 g/dl with a median of 2.7 g/dl. While the minimum level of Albumin on the third day with a minimum value of 0.90 g/dl and a maximum of 3.4 g/dl with a median of 2.5 g/dl.

The SOFA score obtained varies greatly with a minimum value of 1 and a maximum of 11 on the first day with a median of 5.00. The first day CRP/Albumin ratio varied with a minimum value of 7.79 and a maximum of 153.85 with a median of 25.53, while the third day CRP/Albumin ratio with a minimum value of 13.31 and a maximum of 333.33 with a median of 43.16. The use of a ratio between CRP and albumin will provide a variable that can combine the information provided by CRP and Albumin into the index which is positively correlated with infection, i.e., higher ratios indicate higher inflammatory status (Table 2).

Test spearman correlation test showed that the first day CRP/Albumin ratio had no significant relationship with the first day of SOFA score with ($r = -0.062$ and $p = 0.643$). However, the third day of the CRP/Albumin ratio had a significant relationship with the third-day SOFA score with ($r = 0.528$) and ($p = 0.001$) (Table 3).

On the day-1 study, there was 1 (1.7%) patients without organ dysfunction, SOFA score 1 (0-1) with a minimum of 8.61 and a maximum of 8.61. 50 (86.20%) patients experienced organ dysfunction, SOFA 2 scores (2-7) with a first day CRP/Albumin ratio of a minimum of 7.70, a maximum of 153.85 and a median of 26.15. 7 (12.06%) patients experienced organ dysfunction, SOFA 3 scores (8-11) with a day-1 CRP/Albumin ratio of a minimum of 12.74, a maximum of 44.48 and a median of 18.49 (Table 4).

On the day-3 study obtained 16 (27.58%) patients without organ dysfunction with a SOFA score of 1 (0-1) with a day-3 CRP/Albumin ratio of a minimum of 13.31, a maximum of 156.25 and a median of 24.61. 33 (56.89%) patients with organ dysfunction with a SOFA 2 score (2-7) with a day-3 CRP/Albumin ratio of a minimum of 17.55 maximum of 130.43 and a median of 52.46. 7 (12.06%) patients experienced organ dysfunction with a SOFA 3 score (12.06%) with a day-3 CRP/Albumin ratio of a minimum of 37.68 maximum of 333.33 and a median of 99.33. 2 (3.44%) patients experienced organ dysfunction with a SOFA score of 4 (> 11) with a day-3 CRP/Albumin ratio of minimum 33.61 maximum of 166.23 and a median of 99.91 (Table 5).

In calculating the day-1 SOFA score, which had a score of 1 (0-1), there was one patient or 100% who did not experience organ dysfunction on the day-3. There are 50 patients with a SOFA score (2-7), the risk of falling to a score of 4 (> 11) on the third day is 0%. Possibility to risk falling to score 3 (8-11) on the third day is five patients or 10%. Possible risk of falling to a score of 2 (2-7) on the third day was 31 patients or 62%. Possible risk of falling to a score of 1 (0-1) on the third day was 14 patients or 28%.

In SOFA score 3 (8-11) there were seven patients, the risk of falling to a SOFA score of 4 (> 11) on the third day was two patients or 28.6%. The possibility of falling to the SOFA 3 score (3-11) on the third day was two patients or 28.6%. The possibility of risking falling to a SOFA 2 score (2-7) on

**Table 1 Characteristics of subject (n=58)**

| Variable | n (%) |
|---|---|
| Gender | |
| • Males (n%) | 30 (51.7%) |
| • Females (n%) | 28 (48.3%) |
| Ethnic group (n%) | |
| • Batak | 33 (56.9%) |
| • Jawa | 12 (20.7%) |
| • Padang | 5 (8.6%) |
| • Melayu | 3 (5.2%) |
| • Karo | 2 (3.4%) |
| • Mandailing | 3 (5.2%) |
| • Age (Median/ Min / Max) | 55.5 / 18 / 65 |

**Table 2 The characteristics of initial measurement**

| Variabel | Median | Min – Max |
|---|---|---|
| CRP Day-1 (mg/dl) | 70.63 | 23.37- 285.12 |
| CRP Day-3 (mg/dl) | 89.60 | 25.29-300 |
| Albumin Day-1 (g/dl) | 2.7 | 1.3 - 3.8 |
| Albumin Day-3 (g/dl) | 2.5 | 0.9 - 3.4 |
| SOFA score Day-1 | 5.00 | 1 – 11 |
| SOFA score Day-3 | 3.00 | 0.0- 12.00 |
| CRP/Alb ratio Day-1 | 25.53 | 7.79 -153.85 |
| CRP/Alb ratio Day-3 | 43.16 | 13.31 - 333. 33 |

**Table 3 The relationship between CRP/Albumin day-1 and day-3 ratio with day-1 and day-3 SOFA scores**

| Variable | r | P value |
|---|---|---|
| Ratio CRP/ Albumin Day-1 | | |
| • SOFA Day-1 | -0.062 | 0.643 |
| Ratio CRP/ Albumin Day-3 | | |
| • SOFA Day-3 | 0.528 | 0.001 |

**Table 4 The analysis of the relationship between SOFA score day-1 against CRP/Albumin ratio day-1**

| | | Ratio CRP/Albumin H-1 | | |
|---|---|---|---|---|
| Variable | n(%) | Min | Max | Median |
| SOFA Day-1 | | | | |
| 1 (0-1) | 1 (1.7) | 8.61 | 8.61 | - |
| 2 (2-7) | 50 (86.20) | 7.79 | 153.85 | 26.15 |
| 3 (8-11) | 7 (12.06) | 12.74 | 44.88 | 18.49 |

the third day was two patients or 28.6%. Possibility to risk falling to SOFA score 1 (0-1) on the third day is one patient or 14.3%

The results of the analysis of the relationship of dominant organ dysfunction to an increase in the CRP/Albumin ratio are the respiratory system, central nervous system, and kidney system. These results are similar to the results of research conducted by Yoon et al. 2018 that organs that often experience organ dysfunction are the respiratory system, kidney, and central nervous system. So that these elements are obtained by the SOFA score which will be one of the predictors of the outcome

## DISCUSSION

Based in albumin level measurement, this study found a different result compared with study conducted by Farhad et al in 2016 study. The first albumin levels were obtained with a minimum value of 2.2 g/dl and a maximum of 5.6 g /dl. The third-day albumin level with a minimum value of 2.0 g/dl and a maximum of 4.7 g/dl.[16]

At the initial measurement, the minimum CRP level was obtained on the first day with a minimum value of 23.37 mg/dl and a maximum of 285.12 mg /dl with a median of 70.63 mg/dl. This finding is in line with the inflammatory concept of sepsis where physiologically CRP is an acute phase protein produced by liver hepatocyte cells. The CRP synthesis in the liver is very intense and reaches a peak around 24-48 hours. At the same time, the capillary leak will occur in the form of hypoalbuminemia which correlates with the intensity of the inflammatory response triggered by an infection. In contrast to the results of the study of Kim HM et al 2015 where the CRP/Albumin ratio levels of the first 24 hours of ICU care showed a significant relationship with the SOFA score (p = 0.001) and the CRP/Albumin ratio of 72 hours ICU care also showed a significant relationship with the SOFA score. (p = 0.001).[7]

There were a different SOFA score found in our study. A study conducted by Which et al state that if sepsis patients in the ICU get a SOFA score of 0-1, then organ/mortality dysfunction is almost non-existent, but if the SOFA score is > 2 then 10% mortality, SOFA score < 9 then 33% mortality and if SOFA score> 10 then mortality > 95%.[6] Safari et al. also mentioned that SOFA scores > 11 had a mortality rate > 90% and a decrease in this score in 48 hours was associated with a decrease in mortality rate of 6% and if this score did not change or tends to increase then the mortality rate increased by 37% in the initial score 2-7 and 60% if the initial score is 8-11.[11]

The other study conducted by Safari et al were also mentioned that SOFA scores> 11 had a mortality rate> 90% and a decrease in this score in 48 hours was associated with a decrease in mortality rate of 6% and if this score did not change or

**Table 5** The analysis of the relationship between SOFA score day-3 against CRP/Albumin ratio day-3

| Variable | n(%) | Ratio CRP/Albumin H-3 | | |
|---|---|---|---|---|
| | | Min | Max | Median |
| SOFA Day-3 | | | | |
| 1 (0-1) | 16(27.58) | 13.31 | 156.25 | 24.61 |
| 2 (2-7) | 33(56.89) | 17.55 | 130.43 | 52.46 |
| 3 (8-11) | 7(12.06) | 37.68 | 333.33 | 99.33 |
| 4 (>11) | 2(3.44) | 33.61 | 166.23 | 99.91 |

**Table 6** The SOFA score comparison analysis day-1 and day-3

| Parameters | | | SOFA Score Day-3 | | | | Total |
|---|---|---|---|---|---|---|---|
| | | | 0-1 | 2-7 | 8-11 | >11 | |
| SOFA Score Day-1 | 0-1 | | 1 | 0 | 0 | 0 | 1 |
| | | N% | 100.0% | .0% | .0% | .0% | 100.0% |
| | 2-7 | | 14 | 31 | 5 | 0 | 50 |
| | | N% | 28.0% | 62.0% | 10.0% | .0% | 100.0% |
| | 8-11 | | 1 | 2 | 2 | 2 | 7 |
| | | N% | 14.3% | 28.6% | 28.6% | 28.6% | 100.0% |
| Total | | | 16 | 33 | 7 | 2 | 58 |
| | | N% | 27.6% | 56.9% | 12.1% | 3.4% | 100.0% |

**Table 7** The analysis of the CRP/Albumin ratio with the SOFA elements

| Variable | R | P value |
|---|---|---|
| CRP/ Albumin ratio Day-1 – PaO2 / FiO2 Day-1 | -0.201 | 0.131 |
| CRP/ Albumin ratio Day-3 – PaO2 / FiO2 Day-3 | -0.352 | 0.007* |
| CRP/ Albumin ratio Day-1 – GCS Day-1 | 0.164 | 0.218 |
| CRP/ Albumin ratio Day-3 – GCS Day-3 | -0.410 | 0.001* |
| CRP/ Albumin ratio Day-1 – Trombosit Day-1 | -0.048 | 0.722 |
| CRP/ Albumin ratio Day-3 – Trombosit Day-3 | -0.211 | 0.112 |
| CRP/ Albumin ratio Day-1 – Bilirubin Total Day-1 | -0.103 | 0.441 |
| CRP/ Albumin ratio Day-3– Bilirubin Total Day-3 | -0.138 | 0.303 |
| CRP/ Albumin ratio Day-1 – Creatinin Day-1 | -0.179 | 0.179 |
| CRP/ Albumin ratio Day-3 – Creatinin Day-3 | 0.278 | 0.035* |
| CRP/ Albumin ratio Day-1 – MAP/Vasopresor Day-1 | -0.010 | 0.942 |
| CRP/ Albumin ratio Day-3 – MAP/Vasopresor Day-3 | -0.214 | 0.106 |

*Statistically significant (P<0.05)

tends to increase then the mortality rate increased by 37% in the initial score 2-7 and 60% if the initial score is 8-11.[11]

## CONCLUSION

There was a significant positive relationship between the third day CRP/Albumin ratio and the third-day SOFA score. So that it can be used as a predictor of mortality in septic patients in the ICU. The CRP/Albumin ratio associated with SOFA scores can be used as a marker for predictors of mortality in septic patients treated in the ICU.

## ETHICAL CLEARANCE

Ethical approval had been conducted by Ethics of Committee at Universitas Sumatera Utara.


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## CONFLICT OF INTEREST

The authors declare there is no competing interest regarding manuscript.

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## AUTHOR CONTRIBUTION

All authors are responsible as contributor regarding the content of manuscript.

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