Pharmacogn J. 2024; 16(4): 805-808
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Original Article

Association of CRP, Procalcitonin, Lactate, and Albumin Levels with In-Hospital Mortality Post-Definitive Laparotomy in Patients with Complicated Intra-Abdominal Infections

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ABSTRACT

Introduction: Complicated intra-abdominal infection (cIAI) still has a high mortality rate due to organ dysfunction despite advances in supportive care. Unlike other sources of septicemia, cIAI requires source control surgery, which is crucial for improving outcomes. The strategy for source control varies depending on the degree of inflammation associated with cIAI; the more severe the inflammation, the less aggressive the surgery needs to be. Therefore, we need a reliable parameter to predict the degree of inflammation before any physiological rearrangement or organ dysfunction occurs due to excessive inflammation from surgery. The literature shows that CRP, procalcitonin, lactate, and albumin are associated with the degree of inflammation. Thus, it's necessary to study about mentioned parameters for being reference determination strategy of surgery in cIAI, classical definitive laparotomy, or rapid source control laparotomy (RSCL). **Methods:** We have collected data from CIAI patients at Dr. Soetomo Regional General Hospital in Surabaya, Indonesia, covering November 2022 to April 2024. Our primary focus is assessing the inflammation level associated with the compensated or decompensated phase. The decompensated phase signifies an excessive inflammatory response, with one indication being in-hospital mortality. Subsequently, we performed univariate and multivariate analyses using the SPSS program to determine which laboratory parameters (CRP, Procalcitonin, Lactate, and Albumin) are most associated with in-hospital mortality. **Results:** Between November 2022 and April 2024, there were 309 patients with complicated intra-abdominal infections (cIAI). Among the patients, 61.8% were male and 38.2% were female. The majority of patients (27.17%) were aged 61-70. The causes of cIAI included perforated appendicitis (22.65%), perforated peptic ulcer (21.69%), complications from previous surgeries (18.13%), large bowel perforation (12.29%), small bowel perforation (11.33%), intraperitoneal abscess (11.33%), and other causes (2.58%). Statistically, lactate was found to be the most accurate predictor of intraoperative hemodynamic instability (p-value < 0.001; correlation coefficient of 0.481), followed by albumin (p-value < 0.001; correlation coefficient of 0.357). CRP and Procalcitonin were less accurate, with correlation coefficients of 0.182 and 0.272, respectively. The determined cut-off points for lactate and albumin were 1.94 and 2.73, for CRP and Procalcitonin were 23,24 and 47,95. Abnormal laboratory finding in our study mean CRP above cut off point, Procalcitonin above cut off point, lactate above cut off point and albumin below cut off point. More than 2 laboratories finding, in-hospital mortality 66,7%, 2 laboratory finding in-hospital mortality 42,8% and only 1 laboratory finding in-hospital mortality 28,4%. **Conclusions:** CRP, Procalcitonin, Lactate and Albumin have relation statistically significant with in-hospital mortality. Lactate and albumin are better than CRP and procalcitonin in our study, and consider RSCL for more than 2 parameter abnormal laboratory findings CRP, procalcitonin, lactate or albumin.

Keywords: Complicated intraabdominal infection, Inflammatory mediators, Damage control laparotomy.

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History

- Submission Date: 12-06-2024;
- Review completed: 31-07-2024;
- Accepted Date: 13-08-2024.

DOI : 10.5530/pj.2024.16.133

Article Available online

http://www.phcogj.com/v16/i4

INTRODUCTION

Complicated intra-abdominal infections (cIAIs) represent a substantial clinical challenge and serious problem worldwide due to their high morbidity and mortality rates. These infections often necessitate prompt surgical intervention, with definitive laparotomy being a standard procedure aimed at controlling the source of infection and preventing further complications. Despite advancements in surgical techniques and perioperative care, in-hospital mortality rates for patients undergoing laparotomy for cIAIs remain significant [1–3].

In managing cIAIs, early and accurate risk stratification is crucial for optimizing patient outcomes. Biomarkers have emerged as valuable tools in this context, providing insights into the severity of infection and guiding clinical decision-making. C-reactive protein (CRP), procalcitonin, lactate, and albumin have garnered considerable attention. CRP is an acute-phase reactant that rises in response to inflammation, while procalcitonin is more specific to bacterial infections. Lactate levels are indicative of tissue hypoperfusion and metabolic stress, often correlating with the severity of sepsis. Albumin, a negative acute-phase reactant, reflects patients' nutritional and inflammatory status, with low levels associated with poorer outcomes.

Previous studies have explored the predictive value of these biomarkers in various infectious and surgical contexts. However, there is limited comprehensive research specifically addressing their relationship with in-hospital mortality in patients undergoing definitive laparotomy for cIAIs. Understanding

Cite this article: Fardiansyah MS, Lesmana T, Danardono E, Septarendra D, Nugroho I, Wardhana AA, Sugianto A, et al. Association of CRP, Procalcitonin, Lactate, and Albumin Levels with In-Hospital Mortality Post-Definitive Laparotomy in Patients with Complicated Intra-Abdominal Infections. Pharmacogn J. 2024;16(4): 805-808.

these relationships could enhance the clinical management of these high-risk patients, providing a basis for early intervention and tailored therapeutic strategies [4–7].

This study aims to investigate the association of CRP, procalcitonin, lactate, and albumin levels with in-hospital mortality in patients with cIAIs undergoing definitive laparotomy. By elucidating the predictive value of these biomarkers, we seek to improve the risk stratification process and ultimately enhance patient outcomes in this critical population.

METHODS

Data from medical records (physical and computed data) of patients diagnosed with cIAI at RSUD dr Soetomo Surabaya from November 2022 to April 2024 were retrospectively collected. Data that met the inclusion criteria and did not meet the exclusion criteria were collected and recapitulated. Data collected were identity, gender, age, CRP, Procalcitonin, Albumin and preoperative lactate, operative findings, type of surgery, and patient outcome during hospitalization, whether the patient died or not.

Statistical Analysis

The data analysis was performed using the SPSS v23.0 program for Windows. We used the correlation test and the Spearman test for data analysis. Additionally, we utilized ROC curves to identify cut-off points by examining the AUC. Furthermore, we conducted both univariate and multivariate analysis tests.

RESULTS

A total of 309 individuals who were diagnosed with cIAI and had definitive surgery at Dr. Soetomo Hospital between November 2022 and April 2024 were found to exhibit the characteristics above. After that, a descriptive analysis was performed on the total sample to collect patient characteristics, detailed in the following table.

Table 2 below presents the results of a Spearman correlation test. This test aimed to examine the link between the laboratory parameters of CRP, procalcitonin, lactate, and albumin and the probability of death within the hospital. According to the results of the Spearman correlation test, the four laboratory parameter variables had a p-value less than 0.001 and a confidence interval greater than 95%. This indicates that the four variables have a statistically significant relationship. Among the four variables with the strongest link, lactate has the highest correlation coefficient; albumin, procalcitonin, and CRP follow in the order listed below.

Using the ROC curve and looking at the area under the curve (AUC), we were able to determine the moment at which the four laboratory values, CRP, procalcitonin, lactate, and albumin, begin to decrease. Please refer to the figure that follows for further information.

The optimal cut-off point value for predicting in-hospital mortality is shown in Table 5.4. Lactate has the highest sensitivity and specificity of the four variables, with an 86.8 sensitivity and a 78.4 specificity, according to the above table. The study's lactate cut-off point, 1.94, is similar to the typical laboratory result.

This study uses more than one independent variable, so univariate (separate) and multivariate (simultaneous) analyses were carried out, the results are shown in the table 4 below.

Abnormal laboratory finding in our study mean CRP above cut off point, Procalcitonin above cut off point, lactate above cut off point and albumin below cut off point. More than 2 laboratories finding, in-hospital mortality 66,7%, 2 laboratories finding in-hospital mortality 42,8% and only 1 laboratory finding in-hospital mortality 28,4%.

Table 1. Basic characteristic of study subjects by groups.

Variables	Frequency	%
Sex		
Male	191	61,81
Female	118	38,19
Age		
≤ 20 years old	15	4,85
21-30 years old	44	14,24
31-40 years old	38	12,29
41-50 years old	40	12,98
51-60 years old	52	16,83
61-70 years old	84	27,17
≥ 71 years old	36	11,64
Pathology		
Appendic perforation	70	22,65
Perforation of gastric/duodenal peptic ulcer	67	21,69
Small bowel perforation	35	11,33
Large bowel perforation	38	12,29
Intraperitoneal abcess	35	11,33
Related to previous surgery	56	18,13
Others	8	2,58
Outcome		
Inhospital Mortality	74	23,95

(Data were sourced from the medical records of Dr. Soetomo General Hospital)

Table 2. Relationship between laboratory parameters and inhospital mortality.

Variables	Correlation coefficient	p value
CRP	-0,196	< 0,001
Procalcitonin	-0,255	< 0,001
Lactate	-0,373	< 0,001
Albumin	0,310	< 0,001

Table 3. Cutoff points of Laboratory Parameters.

Variables	Cutoff point	Sensitivities %	Specificities %	Baseline normal laboratories
CRP	23,24	55,3	70,3	< 0,3 mg/dL
Procalcitonin	47,95	63,8	67,6	<0,05 ng/dL: normal <0,5: local infection <2: systemic infection <10: severe sepsis >10: septic shock
Lactate	1,94	86,8	78,4	<2 mmol/L
Albumin	2,73	86,0	67,6	<3,5 mg/dL

Table 4. Regression analyses to determine the independent predictor.

Variables	Univariat		Multivariat	
	OR (95% CI)	p value	OR (95% CI)	p value
CRP (mg/dL)	2.926 (1.670 – 5.128)	0.001	2.371 (1.128 - 4.986)	0.023
Procalcitonin (mg/dL)	3.676 (2.111 – 6.402)	0.001	1.936 (0.937 - 4.002	0.074
Lactate (mmol/L)	23.855 (12.205 – 46.624)	0.001	0.626 (0.058 - 6.790)	0.700
Albumin (mg/dL)	12.753 (6.928 – 23.474)	0.001	1.083 (0.368 - 3.184)	0.885

DISCUSSION

The findings of this study demonstrate that preoperative and postoperative levels of CRP, procalcitonin, lactate, and albumin

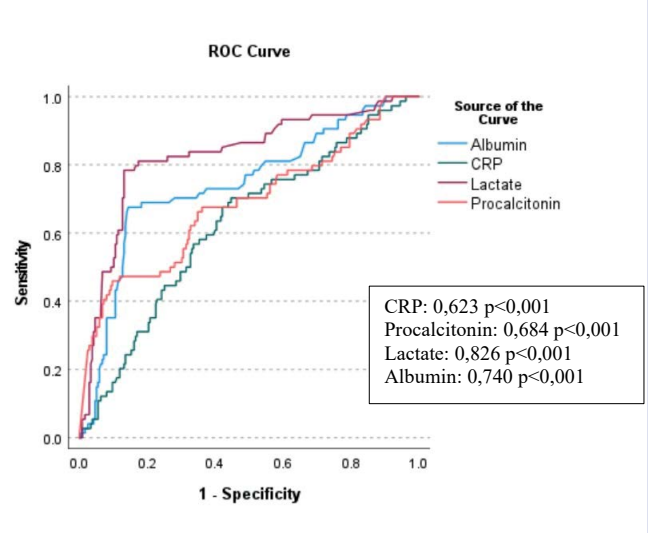

Figure 1. ROC curve of CRP, Procalcitonin, Lactate and Albumin on inhospital mortality.

are significantly associated with in-hospital mortality in patients undergoing definitive laparotomy for complicated intra-abdominal infections (cIAIs). This relationship underscores these biomarkers' critical role in the prognostic assessment of patients with severe intra-abdominal pathology. We have long recognized elevated CRP and procalcitonin levels as inflammation and bacterial infection markers, respectively. In our cohort, both biomarkers were significantly associated with increased in-hospital mortality. However, their predictive power was less robust than lactate and albumin. This finding is consistent with other studies that suggest CRP and procalcitonin are valuable in diagnosing infection. Still, they may be less effective as sole prognostic tools in critically ill surgical patients [8,9].

Lactate emerged as the most powerful predictor of in-hospital mortality in our study. Elevated lactate levels are indicative of tissue hypoxia and metabolic stress, conditions often present in severe sepsis and septic shock. The strong association between high lactate levels and mortality aligns with existing literature, which identifies hyperlactatemia as a critical marker of poor prognosis in various critical illnesses, including cIAIs [6,10–12].

Albumin, parameter of systemic inflammation due to albumin leak to interstitial and also demonstrated significant predictive value for in-hospital mortality. Hypoalbuminemia reflects both a catabolic state and the severity of the systemic inflammatory response. The inverse relationship between albumin levels and mortality observed in our study corroborates previous findings that low albumin levels are associated with worse outcomes in critically ill patients [13–15].

Interestingly, our findings suggest that lactate and albumin levels provide superior prognostic information in cIAIs requiring surgical intervention, despite the widespread use of CRP and procalcitonin in clinical practice to monitor the inflammatory response and guide antibiotic therapy. This is due to several factors that highlight the unique strengths of lactate and albumin as biomarkers in this specific clinical context. CRP and procalcitonin are highly fluctuating, because short half-life within 24 hours. Lactate is a direct marker of tissue hypoxia and metabolic stress. Elevated lactate levels suggest that tissues are not receiving adequate oxygen, a condition often seen in severe sepsis and septic shock, which are common complications in cIAIs. This makes lactate a highly sensitive indicator of critical illness severity and impending organ failure. Numerous studies have shown that elevated lactate levels are strongly associated with increased mortality in critically ill patients. The high predictive accuracy of lactate in predicting adverse outcomes makes it a valuable tool for early risk stratification in patients undergoing surgery for cIAIs. Lactate levels can rise before clinical signs of deterioration become evident, providing an early warning that allows clinicians to intervene promptly and potentially prevent further complications [9,16–18].

While albumin is a parameter systemic inflammation, Hypoalbuminemia, or low albumin levels, indicates a severe systemic inflammatory response, both of which are associated with worse outcomes in critically ill patients. Low albumin levels have been consistently linked to higher mortality rates in various critical illnesses, including cIAIs. Albumin's ability to reflect the overall health and resilience of the patient makes it a strong prognostic indicator. While lactate provides acute insight into metabolic stress, albumin offers a more chronic perspective, showing the long-term impact of illness and inflammation on the patient's body. This dual insight can be crucial in managing and predicting outcomes in complex cases [15,19–21].

By understanding both the acute (lactate) and chronic (albumin) aspects of a patient's condition, clinicians can tailor interventions more effectively, improving patient outcomes. Using lactate and albumin for prognostic purposes can lead to early identification of high-risk patients, timely interventions, improved survival rates, and reduced morbidity. Their ability to provide direct insights into tissue hypoxia, metabolic stress, and overall patient health makes them indispensable tools for improving clinical outcomes in this high-risk patient population. This highlights the importance of a multifaceted approach to patient assessment, integrating various biomarkers to achieve more accurate risk stratification and improve clinical outcomes.

In clinical practice, implementing lactate and albumin measurements as part of the routine assessment for patients undergoing laparotomy for cIAIs could enhance the early identification of high-risk patients. This could lead to timely and targeted interventions, potentially reducing mortality rates. Furthermore, integrating these biomarkers into existing prognostic models may provide a more comprehensive evaluation of patient status and inform decision-making processes in the perioperative period [22,23].

This study's retrospective design and single-center setting may limit the generalizability of the findings. We warrant prospective, multicenter studies to validate these results and investigate the dynamic changes in biomarker levels over time. Additionally, the influence of various confounding factors, such as comorbidities and variations in surgical technique, should be further investigated to refine the predictive utility of these biomarkers.

CONCLUSION

In conclusion, CRP, procalcitonin, lactate, and albumin levels are significantly associated with in-hospital mortality in patients undergoing definitive laparotomy for cIAIs. In our study, lactate and albumin demonstrated superior predictive value compared to CRP and procalcitonin. These findings advocate for incorporating lactate and albumin measurements into routine clinical practice to enhance risk stratification and improve outcomes in this high-risk patient population. Finally, consider RSCL for more than 2 parameter abnormal laboratory findings CRP, procalcitonin, lactate or albumin in our study fashion.

ACKNOWLEDGMENTS

Thank you to the Department of Surgery, Dr Sutomo Hospital Surabaya, Faculty of Medicine, Airlangga University.

FUNDING

No specific funding was provided for this study by the government, businesses, or nonprofits.

DISCLOSURE

Regarding this study, the authors have declared no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Each author committed to take ownership of every aspect of this study and participated in data analysis, article preparation, and paper revision.

ETHICAL CONSIDERATION

This research was approved by the Ethics committee of health research of Dr Sutomo Hospital Surabaya with certificate number 0998/KEPK/V/2024

DATA AVAILABILITY

No extra source data is required as all supporting findings are included in the article.

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Cite this article: Fardiansyah MS, Lesmana T, Danardono E, Septarendra D, Nugroho I, Wardhana AA, Sugianto A, et al. Association of CRP, Procalcitonin, Lactate, and Albumin Levels with In-Hospital Mortality Post-Definitive Laparotomy in Patients with Complicated Intra-Abdominal Infections. Pharmacogn J. 2024;16(4): 805-808.