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Capillary Lactate Level in Non-Severe and Severe Community-Acquired Pneumonia Patients

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Abstract

Background: Community-acquired pneumonia is an inflammatory disease of the lung caused by microorganisms acquired from a non-hospital environment. The pneumonia severity index and ATS/IDSA severity criteria are widely used to predict the severity of CAP. Lactate is a biomarker that can be measured by point-of-care devices that provide results in a short of time. This study aimed to determine the difference in capillary lactate level between non-severe and severe pneumonia to provide an additional method to quickly stratify pneumonia severity and treat it accordingly.

Methods: This cross-sectional study was performed in the emergency room of a regional research hospital. The pneumonia diagnosis was determined by the symptoms, physical examination and radiological findings. Capillary lactate level was measured with Accutrend Plus lactate point-of care device. Severity stratification was done according to ATS/IDSA criteria. The mean of lactate level in all subjects was 3.40±1.52, in non-severe pneumonia subgroup was 2.25±0.94, and 4.56±1.01 in severe pneumonia subgroup. Lactate is significantly higher in severe pneumonia subgroup. The cut-off point of lactate level for severity group was 3.2 mmol/L (95.5% sensitivity, 86.4% specificity).

Conclusion: The early prediction of CAP severity is essential to determine the need for admission in the intensive care unit and close follow up. The lactate level can be used for immediate severity stratification in emergency departments.

Keywords: *lactate; pneumonia; pneumonia severity index*

Introduction

Pneumonia is one of the most common infectious disease causing significant morbidity and mortality, either in developed or developing countries.[1] Its clinical signs are new or progressive infiltrates on chest radiography accompanied by certain symptoms such as cough, sputum production, fever, and shortness of breath.[1,2]

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It is imperative to give antibiotic therapy as early as possible after bacterial pneumonia diagnosis is confirmed to reduce mortality rate.[2,3] Several scoring systems are available to assess pneumonia severity in emergency department, which mostly consist of several clinical sign examination and biomarker measurement.[2,4-7] According to pneumonia severity and close monitoring of clinical response, an appropriate empirical antibiotic determination is crucial to ensure successful management of pneumonia.[8] However, those scoring systems have weakness of requiring venous blood samples, which needs particular expertise, cost, and delayed results.[9]

One of the most frequently utilized biomarkers in infection cases is lactate, which is already used in sepsis management guidelines. Several studies

showed that lactate measurement had clinical utility in initial evaluation and management of pneumonia.[10-17] Several point-of-care devices are available for lactate measurement, which only need microliters of blood. Compared to arterial sampling, capillary sampling is easier to perform, less painful, cheaper, confer faster results, and able to decrease the chance of needle stick injury to health workers.[18] Capillary lactate measurement can be done quickly in busy emergency departments to triage patients according to their severity.[11]

Capillary lactate as severity biomarker in pneumonia is yet to be a routine examination to date. This study aimed to analyze the comparison of capillary lactate between severe and non-severe community-acquired pneumonia patients.

Methods

Subjects

The population of this study was Community-Acquired Pneumonia (CAP) patients admitted into the emergency department of Soetomo General Hospital. Eligible subjects were selected by consecutive sampling method. The inclusion criteria were patients with CAP, over 21 years of age, and willingly participating in the study. The exclusion criteria was patients who had concomitant infection source outside of the lung.

CAP was defined as an inflammation of the lung caused by infectious agents, acquired outside healthcare system, in the patients who had no history of admission in the last 90 days, while having new or progressive infiltrate in chest radiology examination accompanied by supporting clinical symptoms and signs. Pneumonia Severity Index (PSI) was classified according to American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) criteria. Severe pneumonia was defined in patients who had one major criterion or three minor criteria at minimum. The capillary lactate level was measured with Accutrend Plus™ portable lactate device when the patients still in the emergency department.

Ethical clearance

This study follows the principles of the Helsinki declaration. Research ethics has been issued by Dr. Soetomo Hospital Surabaya Ethics Committee (Ethical Clearance Number 684/Panke.KKE/XII/2016) before the start of the study.

Statistical Analysis

The result was analyzed with statistical software package using appropriate statistical significance testing. All data were expressed as means ± SD. Statistical analysis was performed using statistical SPSS software package for Windows, version 17 .0 (SPSS, Inc., Chicago, IL). The comparison of capillary lactate level was analyzed using Independent T-Test for normally distributed interval variables and Mann□Whitney U test for abnormally distributed interval variables.

Results

Characteristic of Pneumonia Severity Index in CAP Patients

It was found that 22 patients was experienced non-severe pneumonia and the other 22 patients had severe pneumonia. Major criteria in severe pneumonia that mostly found was mechanic ventilation utilization with 15 patients (68%), while the minor criteria was respiratory rate ³ 30x/min with 19 patients (86%), and PaO2/FiO2 £ 250 also with 19 patients (86%) (Table 1).

Table 1. Characteristic of Pneumonia Severity Index in CAP Patient

Characteristics	Severe Pneumonia (n=22)	Non-severe Pneumonia (n=22)
Major criteria		
Mechanic ventilation	15 (68%)	0
Vasopressor	7 (32 %)	0
Minor criteria		
Respiratory rate ³ 30x/min	19 (86%)	4 (18%)
PaO2/FiO2 £ 250	19 (86%)	2 (9%)
Multilobar infiltrates	10 (45%)	0
Disorientation	6 (27%)	0
BUN ³ 20 mg/dl	13 (59%)	7 (32%)
White blood count < 4.000 sel/mm3	1 (5%)	0
Platelets < 100.000 sel/mm3	1 (5%)	0
Temperature < 36°C	0	0
Hipotension (Systolic < 90 mmHg)	7 (32%)	0

The difference of lactate level based on major or minor criteria found in severe pneumonia group

There were no significant difference shown in severe pneumonia group which marked by the use of only ventilator; only vasopressor; ventilator combined with vasopressor; and only minor criteria. Therefore, it can be concluded that there was no specific severe pneumonia criteria that affect lactate level dominantly in severe pneumonia (Table 2).

Table 2. The Difference of Lactate Level Based on Major or Minor Criteria Found in Severe Pneumonia Group

Group	Frequency	Mean of lactate level	p-Value (Kruskal Wallis test)
Only ventilator	9	4.54 ± 0.67	0.813
Only vasopressor	1	4.0	
Ventilator + vasopressor	6	4.73 ± 1.30	
Only minor criteria	6	4.5 ± 1.34	

Characteristic of Comorbidities Disease in CAP Patients between Severe Pneumonia Group and Non-severe Pneumonia Group

The comorbidities disease was mostly lung tuberculosis, both in severe pneumonia and non-severe pneumonia groups. The correlation between comorbidities and PSI was p >0.05, hence it can be concluded that there was no significant correlation between comorbidities disease and pneumonia severity index (Table 3)

Table 3. Characteristic of Comorbidities Disease in CAP Patients

Comorbidities	Frequency in Severe Pneumonia	Frequency in Non-severe Pneumonia	p-Value (Fischer exact test)
Tuberculosis	9 (40.9%)	11 (50%)	0.762
Diabetes Mellitus	6 (27.3%)	2 (9.1%)	0.240
Malignancy	4 (18.2%)	5 (22.7%)	1.000
Heart failure	0	2 (9.1%)	0.488
Asthma	0	1 (4.5%)	1.000

The Comparison of Capillary Lactate Level in Comorbidities Disease

The comparison of lactate level in the subjects both with and without comorbidities disease, showed no significant difference with p-value >0.05 (Table 4).

Table 4. The Comparison of Capillary Lactate Level in Comorbidities Disease

Comorbidities Disease	Pneumonia Severity Index	Mean of Lactate on Subject with Comorbidities	Mean of Lactate on Subject without Comorbidities	p-Value
Tuberculosis	Severe	4.644 ± 1.1458	4.500 ± 0.9531	0.751
	Non-severe	2.309 ± 0.9894	2.182 ± 0.9239	0.758
Diabetes Mellitus	Severe	4.967 ± 0.6653	4.406 ± 1.0933	0.257
	Non-severe	2.900 ± 1.2728	2.180 ± 0.9134	0.312
Malignancy	Severe	4.675 ± 1.6460	4.533 ± 0.8852	0.538
	Non-severe	2.480 ± 0.9066	2.176 ± 0.9608	0.537
Heart failure	Severe	---	---	
	Non-severe	3.100 ± 1.8385	2.160 ± 0.8407	0.364
Asthma	Severe	---	---	
	Non-severe	3.2	2.2 ± 0.9343	0.364

Capillary Lactate Level in CAP Patients

The mean of capillary lactate level in community pneumonia patients was higher in severe pneumonia group

than in non-severe pneumonia group. Furthermore, the lactate level in severe pneumonia group had a wider range of value and a bigger variations than in non-severe pneumonia group (Table 5).

Tabel 5. Capillary Lactate Level in CAP Patients

Group	Mean	Minimum	Maximum
All subjects	3.40 ± 1.516	1.1	7.1
Severe pneumonia	4.56 ± 1.012	2.1	7.1
Non-severe pneumonia	2.25 ± 0.936	1.1	4.4

The Comparison of Capillary Lactate Level in CAP Patients between Severe Pneumonia Group and Non-severe Pneumonia Group

The normality test of capillary lactate level in CAP patients was conducted using Kolmogorov Smirnov test, and the result was the capillary lactate level normally distributed with $p > 0.05$. Therefore, to investigate the hypothesis whether any difference of capillary lactate level between severe pneumonia group and non-severe pneumonia group was using Independent Sample T-Test, and the result presented a significant difference with $p < 0.001$. The cut-off point of capillary lactate level with the most optimal AUC, and the highest sensitivity and specificity, to differentiate severe and non-severe pneumonia was found in lactate level of 3.2 mmol/L with AUC of 0.946, sensitivity of 95.5%, and specificity of 86.4% (Figure 1).

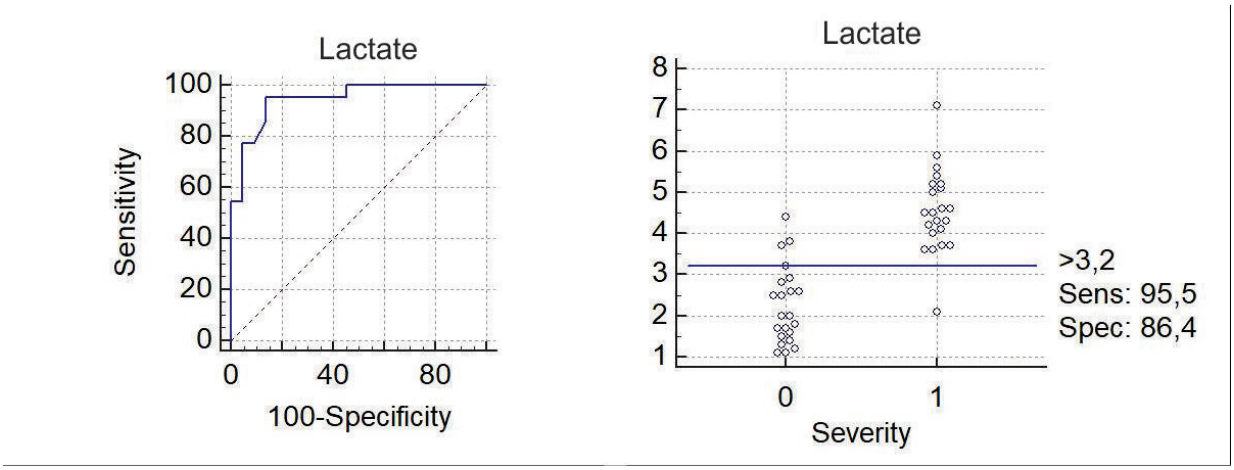

Figure 1. The curve of ROC and dot diagram to determine cut-off point of lactate level

Further analysis was using Cohen's kappa coefficient inter-rater agreement, and the score obtained of Cohen's kappa coefficient was 0.773. It showed that there was a good suitability between the distribution of subjects based on lactate level compared to distribution based on IDSA/ATS criteria to determine pneumonia severity index, which according to Fleiss Cohen's kappa coefficient >0.75 is used to show a good suitability (Table 6).

Table 6. The suitability of lactate level with IDSA/ATS

	Severe Pneumonia	Non-severe Pneumonia	Cohen's kappa coefficient
High Lactate (≥ 3,2 mmol/L)	21 cases	4 cases	0.773 (95% CI 0,587 – 0,959)
Low Lactate (< 3,2 mmol/L)	1 cases	18 cases	

Discussion

In this study, the subjects were distributed into severe pneumonia and non-severe pneumonia group, which was determined based on major and minor criteria of severe pneumonia according to IDSA/ATS. According to the latest ATS guideline for pneumonia, it was mentioned that there are two major criteria and nine minor criteria.

The results presented that the most comorbidities disease was lung tuberculosis, followed by diabetes mellitus, malignancy, and heart failure. Statistical analysis in order to investigate the correlation between comorbidities disease and pneumonia severity index resulted a value of $p > 0.05$. Therefore, it can be concluded that there was no significant correlation between comorbidities disease and PSI in this study. This result proved that despite the comorbidities disease is potentially affect blood lactate level, its insignificant difference of number between severe pneumonia and non-severe pneumonia group could resolve the bias of the cause of the increase in lactate from those comorbidities disease. In line with the study by Demirel, that reported no significant correlation between comorbidities disease and pneumonia severity index in their research.[19]

The result of this study showed the mean of capillary lactate level in subjects was 3.40 ± 1.516 mmol/L, with the mean of capillary lactate level in severe pneumonia group was 4.56 ± 1.012 mmol/L, and 2.25 ± 0.936 in non-severe pneumonia group. This statistical analysis calculation proved that there was a significant difference between both of the groups with $p < 0.001$. The study conducted by Demirel, also found a significant difference between lactate level in died patients and survived patients ($p < 0.001$), with the mean of lactate level in pneumonia was 3.53 ± 3.59 mmol/L, in died patients was 7.76 ± 5.81 mmol/L, and 2.35 ± 0.99 mmol/L in survived patients.[19]

Furthermore, ROC analysis was used to observe the highest cut-off point, sensitivity, and specificity. The highest cut-off point was 3.2 mmol/L with AUC of 0.946, sensitivity of 95.5%, and specificity of 86.4%. Similarly, Demirel found the highest cut-off point was 3.35 mmol/L, AUC of 0.929, sensitivity of 86.4%, and specificity of 88.6%.[19] The cut-off point obtained by this study can be used to help differentiate community-acquired pneumonia patients into severe and non-severe groups and assist in their proper management.

The immune response in pneumonia causes pulmonary ventilation and hemodynamic derangement which result in the decrease of systemic oxygen delivery. Besides, there is also the increase of metabolism causing higher systemic oxygen consumption. The imbalance between the reduction of oxygen delivery and increase of oxygen consumption will increase the systemic oxygen extraction ratio and reduce oxygen saturation. The increase of systemic oxygen extraction ratio above certain tolerance level (50 – 60%) will trigger anaerobic metabolism, which causes higher lactate production. Therefore, lactate concentration is inversely related to systemic oxygen delivery and oxygen saturation and has the ability to reflect pneumonia severity level.[20]

CAP patients in the emergency department are usually in the early phase of hemodynamic disorder, characterized by significantly increased lactate level, but still normal vital signs due to adaptation response of cathecholamine release that prevents shock to occur. This condition is called "occult shock", which can progress to sudden cardiopulmonary collapse. Therefore, lactate

measurement is essential as an early warning marker for detecting that condition.[20]

There are several limitations in this study. First, most of the subject was already treated in prior hospital before being referred, raising the potential bias from the treatment given before the lactate level is measured. Secondly, the diagnostic criteria to differentiate the subject into severe and non-severe group was ATS/IDSA criteria, which has two major and nine minor criteria. Each of them has different underlying pathophysiology that potentially had different effects on lactate level.

Conclusion

This study showed that capillary lactate level had the ability to differentiate CAP patients into severe and non-severe group. The optimal cut-off point for the differentiation is 3.2 mmol/L. Early severity prediction of community-acquired pneumonia is important to decide the effective treatment for patients in the intensive care unit and closer monitoring. Capillary lactate level can be used for quick classification of pneumonia patients in emergency departments.

Conflict of Interest : The authors confirm that this article content has no conflict of interest.

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Author's Contribution: RY and KA designed the study, collected samples, gathered data, analyzed the data, made tables and figures, wrote the manuscript, and contributed to review and revise. All authors have been approved the final version.

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KOMITE ETIK PENELITIAN KESEHATAN
RSUD Dr. SOETOMO SURABAYA

KETERANGAN KELAIKAN ETIK
(" ETHICAL CLEARANCE ")

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KOMITE ETIK RSUD Dr. SOETOMO SURABAYA TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN DENGAN *JUDUL* :

" Perbandingan Kadar Laktat Kapiler pada Pasien Pneumonia Komuniti Derajat Keparahan Tidak Berat dan Derajat Keparahan Berat "

PENELITI UTAMA : Kowiy Akbar, dr

PENELITI LAIN : dr. Resti Yudhawati, Sp. P

UNIT/LEMBAGA/TEMPAT PENELITIAN : RSUD Dr. Soetomo Surabaya

DINYATAKAN LAIK ETIK

SURABAYA, 14 DEC 2016

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