



SERUM LACTATE AS A PREDICTOR OF OUTCOME IN ADULT PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA REQUIRING HOSPITALIZATION

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ABSTRACT

Introduction- Community acquired pneumonia (CAP) is an infectious disease of the lung linked to adverse outcomes. Serum lactate has immense potential in predicting prognosis at admission which may thereby assist clinical decision making and improve patient outcomes. We thus aimed study the role of serum lactate as marker, predictive of outcomes. **Methodology-** This was a single centre, prospective longitudinal study. 55 consecutive patients with CAP matching study criteria were recruited. Patients were subjected to standard of care; venous samples were collected to ascertain serum lactate levels at admission. Analysis of variance (ANOVA) was used to find the significance of study parameters between three or more groups of patients. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. Statistical analysis was done using SPSS software. **Results-** Among the Fifty-Five patients with CAP, the mean age was 55.89 ± 4.84 years and the majority were males. The CURB-65 score did not compare with serum lactate levels, high lactate levels did not necessarily mean high CURB-65 score at admission, $p=0.253$. 68.8% (31/45) of the patients who needed ICU admission had high serum lactate, length of hospital stay and mortality was high among those with serum lactate more than 4mg/dl. **Conclusion-** Serum lactate levels exhibit high potential as a marker for predicting adverse outcomes in CAP, however the differences in our study compared to others, suggest the need for larger, multicentric data to consolidate its role in clinical practice.

KEYWORDS : Pneumonia; Serum Lactate; Predictor; Mortality.

INTRODUCTION

Community acquired pneumonia (CAP) is an acute lower respiratory tract infection developing in non-hospitalized subjects who have abnormal clinical findings on respiratory system examination and radiograph of the chest. Pneumonia is the leading cause of sepsis, which can progress to severe sepsis, septic shock and death. This is a common infectious disease that is associated with significant morbidity and mortality unless treated early with appropriate antibiotic.

CAP is a common disorder with an incidence of about 20% to 30% in developing countries compared to an incidence of 3% to 4% in developed countries¹. The incidence varies markedly with age, being much higher in the very young and the elderly. It is estimated that India together with Bangladesh, Indonesia and Nepal account for 40% of global acute respiratory infection; 90% of mortality is due to pneumonia, mostly bacterial in origin².

CAP mortality is variable, depending on the site of care: it is less than 1% in the outpatient setting, around 5–15% in inpatients not requiring ICU care, up to 25% in intubated patients, and nearly 50% in ICU patients requiring vasopressors³. In the assessment and management of patients with CAP, determination of disease severity is crucial, since it guides various therapeutic options such as the site of care (i.e. need for hospital or ICU admission or suitability for home care), the extent of the microbiological investigation, and the choice and route of empiric antimicrobial chemotherapy. Inpatient treatment of pneumonia is approximately 25 times more expensive per patient than outpatient treatment⁴.

Several tools have been developed to predict mortality and/or assist in determining which patients could be sent home and treated safely with good clinical outcomes. The CURB 65 score is one of the two most extensively studied and validated severity of illness scoring tools. It was derived from the British

Thoracic Society rule, is simple to use, and its accuracy is similar to that of the more complicated scoring systems, such as the Pneumonia Severity Index. Five risk classes are derived from the CURB-65 score, with different predicted mortalities^{5,6}.

Lactate has been used for many years in the assessment of perfusion status and as a measure of illness. Elevated lactate was shown to be independently associated with mortality rate in critically ill patients⁷. Even intermediate initial serum lactate was an indicator of mortality independent of clinically apparent organ dysfunction and shock in severe sepsis patients in the ED. In hospitalized patients, increased lactate indicated high mortality, mechanical ventilation, vasopressor requirement, and a high incidence of ICU admission. Lactate performed well in risk assessment studies in septic patients; the cut-off values (2 and 4 mmol/L) were quite similar in different reports⁸.

The present study aimed to study the outcome of patients with CAP and compare serum lactate levels at admission and thereby ascertain predictive value.

METHODOLOGY:

Source Of Data

The present study was carried out in the Department of Respiratory Medicine, M.S. Ramaiah Medical college and hospitals, Bengaluru. All adult patients with community acquired pneumonia requiring hospitalisation and satisfying study criteria were included in the study.

The research was approved by Ethical committee of M.S. Ramaiah Medical College.

Inclusion Criteria

- Age ≥ 18 years, both male and female
- Two or more symptoms consistent with pneumonia including cough, dyspnoea, fever, sputum production, breathlessness and/or pleuritic chest pain.
- Infiltrates on chest radiograph

Exclusion Criteria

- Patients with pulmonary embolism (PE) or pulmonary oedema.
- Patients positive for HIV or chronically immunosuppressed including those with solid organ transplants, splenectomy or active tumor, or receiving corticosteroids or other immunosuppressive agents.
- Patients diagnosed with Health acquired pneumonia.
- Diabetic ketoacidosis with pneumonia
- Chronic kidney disease with pneumonia
- Chronic liver disease with pneumonia.
- Septic shock due to causes other than pneumonia

Method Of Data Collection

- Study Design- Prospective longitudinal study
- Study duration- November 2015 to June 2016.
- Informed and written consent was obtained from all subjects.
- All patients were subjected to standard of care, their demographic data, vital signs, results of laboratory tests such as complete blood count, arterial blood gas analysis, renal function test, liver function test, random blood sugar and chest radiograph were collected.
- For serum lactate, 5ml of venous blood was collected from peripheral vein without tourniquet in the heparinized vacuum containers at the time of admission to the hospital.
- CURB-65 score was calculated in every patient.

Sample Size

Sample size was calculated using SPSS software based on study by Yun-Xia Chen, Chun-Sheng Li⁸ who observed that the sensitivity and predictivity of serum lactate level in predicting outcome was 68%. In our present study expecting similar results with 10 % relative precision and to get 95% confidence in the result, the study requires minimum of 55 subjects.

Outcome Measures:

- Primary outcomes
 - In Hospital Mortality
- Secondary outcomes
 - Ward admission and ICU admission
 - Need for Vasopressors
 - Need for mechanical ventilation
 - Need for Non-invasive ventilation
 - Length of hospital stay- calculated by subtracting the hospital admission date from the hospital discharge date.

Statistical Analysis

Statistical Methods:

Descriptive and inferential statistical analysis was employed in this study. Results on continuous measurements were presented as Mean $\pm$ SD (Min-Max) and results on categorical measurements were presented as Number (%). Significance was assessed at 5 % level of significance.

Analysis of variance (ANOVA) was used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Fifty-Five consecutive patients admitted with a diagnosis of CAP and satisfying study criteria were recruited. Their baseline characteristics are outlined in table 1. The mean age of the study population was 55.89 ± 4.84 years, the majority were males ($n=34/55$) and belonged to the age group of 50-70 years ($n=33/55$). The majority presented with cough, dyspnea and fever, while hemoptysis was the least common complaint, table 1. Diabetes mellitus and systemic hypertension were the most common comorbid conditions in this study population, table 1.

At admission, 85.5% were tachypneic and 81.8 % were hypoxic, other signs are summarized in table 2. Of the 55 subjects, 81.8 % needed intensive care unit admission (ICU), where 56.4% needed NIV and 6% needed intubation during their course of illness, table 3. At admission, blood analysis revealed anemia (52.7 %) and leukocytosis (78.2 %) in the majority, table 4. Serum lactate was elevated in 63.6 % of all cases, table 4.

On Sputum examination, bacterial growth on culture was seen in only 7 cases (12.7 %) growth of klebsiella species was seen in 3.6%, staphylococcus aureus in 3.6%, acinetobacter in 1.8%, E.coli in 1.8% and pseudomonas in 1.8% patients. In addition, Ziehl Neilson stain for Acid Fast Bacilli was positive in 4 cases.

On Chest radiograph, 43.65% ($n=24$) had bilateral infiltrates, 38.17% ($n=2$) had infiltrates on the right side and 18.16% ($n=10$) had infiltrates on the left side.

The CURB-65 score did not compare with serum lactate levels, high lactate levels did not necessarily mean high CURB-65 score at admission, $p=0.253$, table 3. On the other hand, 68.8% (31/45) of the patients who needed ICU admission had high serum lactate, more predominantly in the moderate risk group. The mean length of hospital stay was the most when serum lactate was between 2-4mg/dL, this difference attained moderate statistical significance, $p = 0.012$, table 3. Three cases succumbed to their illness, where 2 had serum lactate levels above 4mg/dl, this difference attained strong statistical significance with p value = 0.008, table 3.

DISCUSSION

Community-acquired pneumonia refers to pneumonia acquired within the general community and is defined as an acute infection (of less than 14 days duration) associated with inflammation of the lung parenchyma distal to the terminal bronchioles, most commonly bacterial in nature, and associated with clinical and/or radiological evidence of consolidation of part or parts of one or both lungs⁷.

Severity of illness assessment of patients with CAP presenting to an ED impacts on decisions regarding the site of care, the extensiveness of the microbiological and laboratory evaluation, the type, route, and duration of antibiotic therapy, the intensity of clinical observation and the overall medical resource use for this condition.

Accurate prognostication helps to predict the expected outcomes and the probability of serious adverse events in the initial management decisions.

The mean age of the patients in this study was 51 to 60 years (55.89 ± 4.84). Similar (52.7 ± 18.1) distribution were seen in studies by S. Bansal et al⁹ and Chen YX et al⁸ reiterating the higher incidence of pneumonia among the relatively elder population. These studies also showed higher male preponderance in their study population, similar to ours.

With regard to the outcome of patients studied; 52 survived and recovered while 3 died. Two patients in the study group

died due to pneumonia and septic shock, and one died due to pneumonia and sepsis, multiorgan failure and associated underlying uncontrolled diabetes mellitus. The secondary outcomes in the remaining patients noted as ICU admission in (81.81%), ward care (18.18%), Need for NIV in (56.4%), mechanical ventilation in (10.9%) and Vasopressors in (16.4%) cases.

Pneumonia independently predicts 28-day in-hospital mortality in septic patients admitted to the intensive care unit (ICU). Elevated lactate was shown to be independently associated with mortality rate in critically ill patients¹⁰. Even intermediate initial serum lactate was an indicator of mortality independent of clinically apparent organ dysfunction and shock in severe sepsis patients in the Ed¹¹.

Analysis of Serum lactate among patients in the study revealed lactate level of <2 (mmol/l) in 36.4 patients, 2-4 in 54.5%, and >4 in 9.1% patients, on the other hand when patients were subjected CURB-65 score of patients; 47.3% of them had score <1, 40% had score 2, and 12.7% had >3 in 12.7%.

Primary Outcome :

Mortality- In our study there was a death of one patient in low risk category i.e. lactate level below 2mmol/L and 2 patients in high risk (40%). The sensitivity and specificity of serum lactate in predicting mortality in our study could not be estimated because of low mortality rate. However, mortality occurred in 2 patients in high risk group, this difference attained statistical significance, $p=0.008$, however needs cautious interpretation in view of the relatively low sample size. A large cohort study by Chen Y-X et al⁹ found that sensitivity and specificity of serum lactate in predicting mortality were 68% , 82% respectively for the 3 risk groups & the cutoff level of lactate was 4 mmol/L. Houman Khosravani et al¹², studied occurrence and adverse effect of outcome of hyperlactatemia and found that lactate more than 2mmol/L carried high risk of mortality among medical critically ill patients admitted to ICU.

The result of our study provided some evidence that mortality rate could be predicted by measuring lactate on ED arrival in adult patients in relatively severe pneumonia.

Secondary Outcome:

- Ward and ICU admission- In our study with regard to serum lactate in correlation to the ICU and ward admission, it was found that those in moderate risk group in 90% (27 patients) needed ICU admission, compared to other risk groups, table 3. Chen Y-X et al⁹ observed that the rate of ICU admission rapidly increased to 39% in patients with lactate above 4 mmol/L, the difference being a significantly higher no of patients with a lower lactate level. This result demonstrated that lactate above 4 mmol/L is a strong indicator of ICU admission in pneumonia patients in the ED.
- Need for Vasopressors- Those patients in the high risk group needed vasopressors, more than other groups, table 3. Tang Y et al¹³ in their study on patients with severe sepsis concluded that serum lactate levels of 2-4 and >4mmol/l were more likely to need vasopressors support as seen in 12.9% of cases.
- Need for mechanical ventilation and Non-invasive ventilation- in this study those patients in the high risk group were more likely to need NIV or mechanical ventilation, table 3. WY Kim et al¹⁴, in their study on patients with pneumonia and sepsis found that when 58% of patients needed mechanical ventilation and 40% needed when serum lactate ≥ 3.5 mmol/l.
- Length of hospital stays in relation to risk of serum lactate and CURB-65- LOHS was highest in the moderate risk group, this difference attained statistical significance between the groups, $p=0.012$, on the other hand the

difference when grouped by CURB -65 scoring was not significant, $p=0.053$, table 3. Houman khosravani¹² observed higher LOHS with higher serum lactate level, our study had higher mortality in the high risk group and relatively low sample size, hence the difference between the studies.

The limitations of this study include small sample size, Single center study and relatively small duration of study.

CONCLUSION

Serum lactate levels exhibit high potential as a marker for predicting adverse outcomes in CAP, however the differences in our study compared to others, suggest the need for larger, multicentric data to consolidate its role in clinical practice.

Table 1- Baseline characteristics

Variable	Frequency (n)	%
Age Category		
<30 years	3	5.5
31 to 40 years	8	14.5
41 to 50 years	3	5.5
51 to 60 years	19	34.5
61 to 70 years	14	25.5
71 to 80 years	6	10.9
>80 years	2	3.6
Total	55	100
Gender		
Males	34	61.8
Females	21	38.2
Symptoms		
Cough	55	100.0
Dyspnoea	53	96.4
Fever	52	94.5
Wheeze	35	63.6
Chest pain	21	38.2
Loss of appetite	7	12.7
Weight loss	6	10.9
Hemoptysis	5	9.1
Co-morbid conditions		
Diabetes Mellitus		
Hypertension	32	58.2
COPD	25	45.5
Ischaemic Heart Disease	17	30.9
	6	10.9
Physical Examination		
Pallor	36	65.45
Clubbing	7	12.7
Confusion	5	9.1
Edema	3	5.5
Cyanosis	2	3.6
Icterus	2	3.6
Lymphadenopathy	0	0.0

Table 2- Vital signs at admission

	Frequency (n)	%
Heart rate (bpm)		
<70	0	0.0
70-110	47	85.5
>110	8	14.5
SBP (mm Hg)		
<90	09	16.3
90-120	17	30.9
>120	3	5.5
DBP (mm Hg)		
<60	12	21.8
60-100	42	76.3
>100	1	1.8
RR		
<30	5	9.1
30-40	47	85.5
>40	3	5.5

SpO2%		
<80	1	1.8
80-90	44	80.0
>90	10	18.2
Temperature (°F)		
<98	0	0.0
98-101	50	90.9
>101	5	9.1

Table 3 Serum lactate and outcome parameters.

Serum Lactate	Low Risk (<2)	Moderate Risk (2-4)	High Risk (>4)		P value
CURB-65	Frequency n(%)			Total	P=0.253
Score 0	2(100%)	0	0		
Score 1	11(45.8%)	12(50%)	1(4.2%)		
Score 2	4(18.2%)	15(68.2%)	3(13.6%)		
Score 3	1(50%)	1(50%)	0		
Score 4	2(40%)	2(40%)	2(40%)		
Total	20(36.4%)	30(54.5%)	5(9.1%)		
Admission status	Frequency n(%)			Total	
To ICU	14 (70%)	27 (90%)	4 (80%)	45(81.8%)	
To Ward	6(30%)	3(10%)	1(20%)	10 (5%)	
Total	20 (100%)	30 (100%)	5(100%)	55(5%)	
Need for Non-invasive ventilation	Frequency n(%)				
Yes	8 (40%)	19 (63.3%)	4 (80%)	31(56.4%)	
No	12 (60)	11 (36.7%)	1 (20%)	24(43.6%)	
Total	20 (100%)	30 (100%)	5 (100%)	55(100%)	
Need for mechanical ventilation	Frequency n(%)				
Yes	1 (5%)	3 (10%)	2(40%)	6 (10.9%)	
No	19 (95%)	27 (90%)	3 (60%)	49(89.1%)	
Total	20 (100%)	30 (100%)	5 (100%)	55 (100%)	
Need for Vasopressor support	Frequency n(%)				
Yes	1 (5%)	6 (20%)	2 (40%)	9 (16.4%)	
No	19 (95%)	24 (80%)	3 (60%)	46(83.6%)	
Total	20 (100%)	30 (100%)	5 (100%)	55 (100%)	
Mortality	Frequency n(%)				P=0.008
Yes	1(5%)	0(0%)	2(40%)	3	
No	19(95%)	30(100%)	3(60%)	52	
Total	20(100%)	30(100%)	5(100%)	55	
Length of hospital stay	Mean $\pm$ SD				
	6.75 $\pm$ 3.9	10.27 $\pm$ 5.0	5.40 $\pm$ 4.0		P=0.012
	3	0	4		*

Table 4- Results of blood investigations at admission.

Variable		
Haemoglobin (g/dl)	Frequency (n)	%
<12	29	52.7
12-16	24	43.6
>16	2	3.6
Total Leucocyte count (cells/ mm3)	Frequency (n)	%
<4000	4	7.3
4000-11000	8	14.5
>11000	43	78.2
ESR	Frequency (n)	%
<35	4	7.3
35-60	37	67.3
>60	14	25.5
RBS	Frequency (n)	%

<180	21	38.2
180-260	32	58.2
>260	2	3.6
BUN (mg%)	Frequency (n)	%
<19	27	49.1
>19	28	50.9
Serum Creatinine (mg/dl)	Frequency (n)	%
<1.1	27	49.1
>1.1	28	50.9
Serum Lactate (mg/dl)	Frequency (n)	%
<2	20	36.4
2-4	30	54.5
>4	5	9.1
Arterial Blood Gas Analysis	Frequency (n)	%
Ph		
<7.3	6	10.9
7.3-7.4	24	43.6
>7.4	25	45.5
Pco2		
<35	8	14.5
35-45	39	70.9
>45	8	14.5
PO2		
<70	21	38.2
70-90	31	56.4
>90	3	5.5
HCO3		
<18.5	14	25.5
18.5-25	37	67.3
>25	4	7.3

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